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BRAIN.

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INTRACRANIAL AND SPINAL METASTASES IN GLIOMAS OF THE BRAIN.

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THE discovery of spinal metastases from a cerebral glioma in the first case described in this paper led us in 1928 to make a routine examination of the spinal cord in all cases of intracranial tumour, and as a result unexpected lesions of the spinal cord and its membranes have been brought to light. The frequency with which intracranial tumours are accompanied by tumours or other lesions in the spinal cord has in the past been greatly under-estimated. Our cases show clearly that no true indication of the frequency is given by clinical examination alone.

Lesions of the spinal cord that may be encountered at necropsy in cases of intracranial tumour are given in Table I. Most of these combinations have been encountered by us, and for the others references are given. The table could doubtless be amplified with increased experience. Examples of Groups 7, 8 and 9 provide interesting material illustrating the relationship of neurofibromas to meningiomas and gliomas. We are concerned here only with Groups 1 to 5. It has for some time been known that medulloblastoma of the vermis frequently gives spinal metastases or spreads directly into the spinal subarachnoid space. The fact that other varieties of glioma may give rise to similar metastases has not hitherto been emphasized. It seems, however, from the cases presently to be described that in special circumstances all varieties of glioma can give rise to metastases.

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[2] Working under grants from the Medical Research Council.

TABLE I.—SPINAL LESIONS ASSOCIATED WITH INTRACRANIAL TUMOURS.

Brain	Spinal cord
1. Primary cerebellar glioma	Secondary glioma, by extension in continuity through foramen magnum
2. Primary cerebral glioma	Metastatic spinal glioma
3. Metastatic cerebral glioma (from glioma of retina)	Metastatic spinal glioma
4. Metastatic cerebral glioma	Primary spinal glioma [15]
5. Sarcomatosis of meninges	Sarcomatosis of meninges [17]
6. Primary cerebellar angeioma	Primary spinal angeioma [14]
7. Primary intracranial meningioma	Primary or ? metastatic spinal meningioma
8. Neurofibromatosis of roots of cranial nerves	Neurofibromatosis of roots of spinal nerves
9. Combinations of 7 and 8, with or without spinal glioma	
10. Primary melanomatosis	Primary melanomatosis [10]
11. Pituitary adenoma	Metastatic pituitary adenoma [1]
12. Metastatic carcinoma or sarcoma	Metastatic carcinoma or sarcoma
13. Primary intracranial tumour	Syringomyelia [13]

[1] A female, aged 25 (P.M. 153, 1931), who died in coma with hyperglycæmia, was found to have a large, very soft pituitary adenoma projecting into the base of the brain. During life it was observed that the cerebrospinal fluid contained cells of a peculiar type that were not identified. On naked-eye examination of the dorsal surface of the spinal cord a slight milky or rusty opacity of the pia arachnoid was observed in two places and there was a little reddish brown deposit at the extreme tip of the cauda equina. Microscopic examination of these areas revealed in the subarachnoid space among extravasated red corpuscles scattered, frequently multinucleated, cells which were identical with those composing the primary tumour. There was no indication of a multiplication of these cells *in situ*, nor did they appear to be in any way grafted on to the structures in their environment. No surgical procedure other than lumbar puncture had been done in this case.

HISTOLOGICAL METHODS.[1]

In the cases that follow, the material was fixed in 4 per cent. saline formaldehyde. Paraffin sections were stained with hæmatoxylin and eosin, iron hæmatoxylin and van Gieson's mixture, Weigert's fuchselin and neutral red, Laidlaw's silver method for reticulum, and, after treatment with Zenker's fluid, with Mallory's phosphotungstic acid hæmatoxylin. Frozen sections were stained by Herxheimer's method, and by Penfield's modification of Cajal's gold chloride-sublimate method, and of Hortega's silver carbonate methods for oligodendroglia and astrocytes. In addition the Marchi and Weigert Pal methods were employed in the examination of the cord in Case 2.

Where material was obtained by surgical operation, portions were fixed in Zenker's fluid and in formalin-ammonium-bromide as well as in formaldehyde, unless otherwise specified.

NOMENCLATURE.

Bailey and Cushing's classification [4] has been used in naming the different types of glioma encountered. In Case 1 the tumour differed histologically from any recognized type, and it has been decided temporarily to leave it unclassified.

[1] The lists of tissues examined histologically in individual cases have been omitted to save space.

Report of Cases.

Case 1.—*Glioma (unclassified) of third ventricle. Negative cerebellar exploration. Right transfrontal operation and biopsy. X-ray treatment. Death.*

History: Winifred B., aged 9, referred by Dr. Riddoch, was first seen on July 7, 1928, when she complained of attacks of right frontal and temporal headache and vomiting which had begun eight weeks before. These attacks lasted about a day, and in one of them she had been semiconscious for twenty-four hours and during that time had head retraction. Six weeks before admission she had come to her mother complaining of an unpleasant sensation in her right upper limb, and her mother observed that her left leg was shaking, and that she had some difficulty in speaking. This attack lasted about half an hour. From that time she began to suffer from almost continuous and often severe pain in the right knee and hip. Slight epistaxis had occurred from the right nostril at intervals during the illness. She had been quite steady in walking and there had been no disturbance of vision.

Examination: The patient was an intelligent and cheerful child, but during attacks of headache she became very irritable, and for several minutes at a time would show intense pallor of the face accompanied by slowing of the pulse-rate down to 60. Occasionally during these attacks she complained of feeling "hot all over." There was an engorged subcutaneous vein on the bridge of the nose. The fundi showed bilateral papilloedema (right, 1·5 D.; left, 2 D.). On one occasion during headache there was temporary complete left temporal hemianopia to 2/2000 and a relative left temporal scotoma to 5/2000 white, which in the light of subsequent events was probably caused by a temporary pressure on the right optic tract. The left pupil was slightly enlarged. There was slight weakness of the right side of the face and of the right lower limb. The reflexes on the right side were normal, but on the left side the lower abdominal reflex was diminished and the plantar reflex was extensor. She was slightly unsteady in walking when turning to the left, but showed no other sign of inco-ordination. There was generalized hypotonia. Passive movement of the right knee and hip was painful but not limited, and X-rays of this region showed no abnormality. Sudden twisting of the trunk produced sharp pain in the region of the right anterior superior iliac spine. In this region also there was an ill-defined area of cutaneous tenderness, but at that time no other change of sensibility was observed.

X-rays of the skull showed widening of the sutures, moderate enlargement of the sella turcica with erosion of all the clinoid processes and thinning of the dorsum sellæ. By lumbar puncture a slightly yellow cerebrospinal fluid was obtained which contained 0·5 per cent. of protein, and seven white cells per cubic millimetre.

Diagnosis.—It was clear that there was an intracranial tumour which probably occupied either the third or the fourth ventricle. The bilateral pyramidal signs and the attacks of pallor of the face associated with

bradycardia were considered to favour a diagnosis of tumour of the third ventricle, but it was thought at that time that the pain in the right thigh and the changes in the cerebrospinal fluid were against this diagnosis and in favour of a tumour of the fourth ventricle. For these signs were regarded as being probably due to metastases in the spinal subarachnoid space, a complication well known to occur in cases of medulloblastoma, a glioma that is found almost exclusively (Cushing [7]) in the vermis of the cerebellum.

The patient was observed for a period of seventeen days, and during that time she developed double vision, and nystagmus at the extremes of lateral and upward movement of the eyes. An attack of coarse tremor of the right lower limb occurred which lasted fifteen minutes. At its height there appeared a fine tremor of the right upper limb, and a few involuntary movements of the muscles of the right side of the neck. She could move her limbs freely and her speech was not affected, and though she became quite pale she did not seem to be greatly distressed. During this attack the weakness of the right side of the face was accentuated.

The pain in the right lower limb persisted, but its area of maximum intensity shifted to the knee. She began to show a distinct limp when walking. Repeated examinations were made by Dr. Riddoch, Dr. Russell Brain and others to elicit more definite signs of spinal tumour, but the only signs obtained were slight cutaneous tenderness from the tenth thoracic to third lumbar segmental areas, diminution of all abdominal reflexes and of the right knee-jerk, limitation of extension of the lumbar part of the spinal column, and slight tenderness of the lower lumbar and upper sacral spinous processes.

On July 24 she began to have frequent and violent attacks of headache and vomiting, and during the night became delirious and unmanageable. It was decided to explore the fourth ventricle.

First operation, July 25, 1928: Ether anæsthesia. Cerebellar decompression was performed through the usual crossbow incision. The cerebellar tonsils were not displaced downwards and were so widely separated that by gentle retraction the whole of the lower half of the fourth ventricle could be seen. It was quite free from tumour. At an early stage of the operation both lateral ventricles were tapped and were found to be dilated. Subsequently, pressure on the cerebellum resulted in the escape of only a small quantity of fluid from the needles in the lateral ventricles. The fluid collected from the lateral ventricles, quite unlike that previously obtained by lumbar puncture, was colourless and contained only 0·08 per. cent. of protein and 1 white cell per cubic millimetre.

For two weeks after this operation the patient improved, but then she became drowsy and began to vomit once more. An attack occurred of clonic movements in the left lower limb. It was preceded by a sensation of falling and was accompanied by intense pallor of the face. It lasted two and one half minutes. Consciousness and speech were retained during the attack.

Second operation, August 16, 1928: Ether anæsthesia. In a further attempt to expose and remove the tumour, the region of the third ventricle was exposed by the right transfrontal route. On the outer aspect of the right optic nerve and right internal carotid artery a soft vascular process of tumour was found. This extended backwards towards the third ventricle, which felt unusually firm as if occupied by tumour. It was obviously impossible to remove the tumour completely and nothing was done beyond removing some fragments for histological examination. This showed a cellular glioma.

Subsequent course: The immediate post-operative course was uneventful except that the patient became incontinent of urine. As her condition was obviously desperate, an intensive X-ray treatment to the third ventricle was given seven days after operation. About fifteen hours later there was very great increase of intracranial pressure. The patient became unconscious and died on the following day. It is evident that the initial dose of X-rays should have been very much smaller, even though a cerebellar decompression had already been made.

Summary of Necropsy. (*P.M.* 386, 1928.)

Glioma (unclassified) of third ventricle. Secondary glioma of spinal subarachnoid space. Operations: cerebellar decompression; right transfrontal exploration and partial removal of tumour. Chronic focal descending nephritis. Petechial hæmorrhage in pericardium of margo obtusa. Slight anthracosis of lungs. Dilatation and post-mortem digestion of lower half of œsophagus. Mucous catarrh of stomach. Œdema and congestion of liver and spleen. Slight injection of synovial membrane of right acetabulum. Very slight atheroma of mitral valve and aortic commissure. Patent foramen ovale. A thin, well developed girl.

Macroscopic Examination.

Brain.—The brain was fixed *in situ* and removed eighteen hours after death. On sagittal section the lower anterior part of the third ventricle was found to be filled with a mass of tumour, measuring 3·2 by 2·3 by 2·0 cm., which projected up into the upper part of the ventricle between the anterior and middle commissures and elsewhere was attached to its walls. It lay immediately above the sella turcica, and the diaphragma sellæ presented a corresponding shallow cup-shaped depression. The tumour was firm, of the consistence of rubber, and its cut surface was grey or white and flecked with pin-point and linear red areas. It extended into the leptomeninges over the floor of the third ventricle and enclosed the optic chiasm and adjacent internal carotid arteries. A layer of grey tumour tissue, up to 0·3 cm. deep, covered the cerebral peduncles and spread backwards over the front of the pons and the adjacent cerebellum. The posterior communicating and posterior cerebral arteries, and the origins of the third to eighth cranial nerves on each side were obscured by this layer of tumour, but the basilar and vertebral arteries were superficial to it. The arachnoid membrane which covered them was white and opaque.

The arachnoidea over the convex surfaces of the cerebral hemispheres presented in places a faint milky-white appearance. The body and occipital horn of the left lateral ventricle showed a patchy, thin red deposit on their walls. The lateral ventricles were moderately dilated.

Spinal cord.—The posterior surface of the spinal cord presented a normal appearance down to the eighth cervical segment, but below that it was everywhere covered by a layer of greyish-white tumour tissue up to 0·25 cm. deep. There was slight opacity of the arachnoid membrane over the upper part of the cauda equina; below this the lower end of the spinal subarachnoid space was completely filled with a solid conical mass of tumour tissue, 1·3 cm. diameter. The anterior surface of the spinal cord for the most part retained its normal pattern, but showed a few patches of tumour tissue, up to 1·0 by 0·5 cm.; on the cauda equina there was a large white plaque of tumour, 2·0 by 1·2 cm., attached to the deep surface of the arachnoidea.

Microscopic Examination.

The primary tumour.—The tumour in the third ventricle is of somewhat loose texture and is subdivided by a wide-meshed network of collagen and small blood-vessels (fig. 1). The tumour cells lying in the spaces so formed lie parallel to one another in small bundles. In hæmatoxylin and eosin preparations the cytoplasm of these cells is difficult to observe: the groups of nuclei appear to be separated by a spongy network of fine eosinophil cytoplasmic threads. But in preparations stained with phosphotungstic acid hæmatoxylin it is clear that most of the cells are of tadpole shape and possess a simple long, tapering, finely-fibrillated process. In a group of cells the processes are given off in the same direction and stream in a leash towards a neighbouring blood-vessel or strand of collagen. In the upper half of the tumour and in a triangular zone adjacent to the leptomeninges covering its lower border, where the tissue appears to be best preserved, this palisading of the nuclei and the fibrillated character of the cell processes is very clear (fig. 2). Although the processes tend to radiate towards blood-vessels, there is no suggestion of the formation of foot-plates, nor is the arrangement definite enough to recall the perivascular "pseudo-rosettes"[1] of Bailey found in the more highly differentiated types of glioma, such as ependymomas and astroblastomas.

The nuclei are oval and of even size. They have a deeply-stained and well

[1] Much confusion exists over the use of the term "rosette" in connection with gliomas. Flexner [11] applied it to an arrangement of cells in neuro-epithelioma of the retina. In this the cells appear in section to be collected about a central lumen. Wright [22] again used the term to describe the arrangement seen in the so-called neuroblastoma, whereby the cells appear to be grouped in a circle the centre of which is occupied by their cytoplasmic processes. Bailey [1] and others give the name of "pseudo-rosette" to a perivascular arrangement of cells in which the cell processes are directed to the vessel wall, and also to the rosettes of Wright. They also broaden Flexner's definition of rosette to include cell formations in which the cytoplasmic border of the lumen is occupied by cilia and blepharoplasten. In this paper any terms used are qualified by the name of the author who first applied that term to that particular structure.

defined nuclear membrane and a fine chromatin net, with from one to four nucleoli and a number of small nodes of variable size. The nuclei do not appear as rich in chromatin as the nucleus of the medulloblast, as seen in typical medulloblastomas. No blepharoplasten are seen in the cytoplasm. Although nearly all the cells are of unipolar form, a few are less well differentiated; these show short blunt processes extending from one or both poles, or, more rarely, five or six short processes arranged in stellate fashion. The cells of the tumour are not impregnated by the gold chloride-sublimate method of Cajal. No giant cells and no mitotic figures are seen.

The reticulum is confined to the meninges and to the walls of the blood-vessels. In the periphery of the tumour, in one area, are numerous small

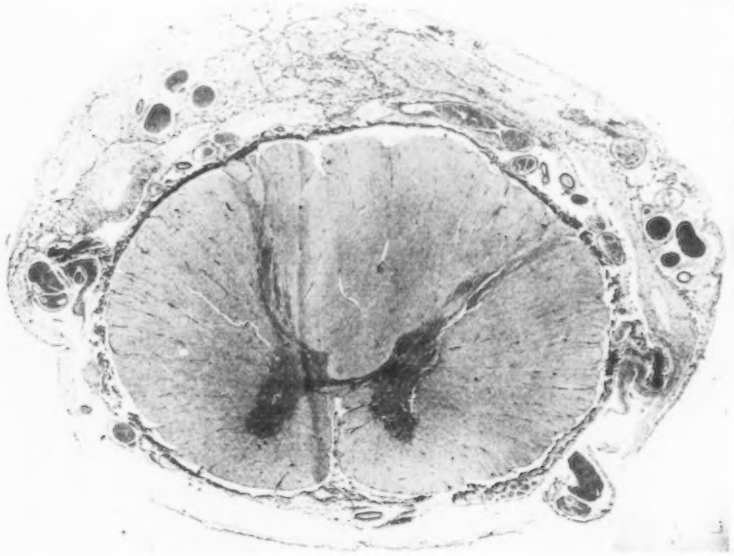

FIG. 3 (*Case* 1).—Spinal cord at eighth thoracic segment. The subarachnoid space over the dorsal and lateral aspects of the cord is filled with tumour. Phosphotungstic acid hæmatoxylin. × 9.

hæmatoxyphil spheres of "calcification." The leptomeninges covering the lower border of the tumour are thickened by invading tumour cells and by a fibroblastic proliferation. The tumour cells here are less closely packed, and their form and disposition can be clearly seen.

Intracranial extensions.—The leptomeninges of the medulla and adjacent cerebellum are extensively infiltrated with tumour cells of the same unipolar form, and the tumour extends into the sulci of the cerebellum. There is also slight infiltration of the leptomeninges of the left temporal cortex. There is no invasion of the nerve tissue or of the perivascular spaces of perforating

vessels. Over the left Rolandic cortex there is slight fibrous thickening of the leptomeninges without infiltration by tumour. Beneath the ventricular ependyma there are a few recent perivascular hæmorrhages but no evidence of tumour.

Spinal metastases.—The subarachnoid space over the dorsal and lateral aspects of the cord is occupied by a crescentic mass, up to 3 mm. thick, of tumour cells and interlacing strands of collagen and reticulum (fig. 3). The reticulum is abundant, but there are occasional small islands of tumour cells that are free from reticulum. The tumour cells are identical with those found in the cranial meninges, and they do not infiltrate the substance of the cord. There is considerable focal degeneration and necrosis of these cells, associated with leucocytic and plasma cell infiltration.

Comment.—The tumour is a glioma of embryonic type. In its diffuse spread through the leptomeninges there is close macroscopic resemblance to medulloblastoma. It is, however, more differentiated than the typical medulloblastoma, and it contains very few cells that could be regarded as medulloblasts. Moreover, the absence of mitotic figures and of giant cells, the presence of nodules of calcification in the margin of the primary tumour, and the conspicuous production of collagen and reticulum in the infiltrated parts of the leptomeninges indicate a tumour of slower growth than medulloblastoma. The type of cell is a unipolar spongioblast with fibrillated cytoplasm (fig. 2). The absence of blepharoplasten differentiates it from an ependymal spongioblast, and the absence of vascular expansions distinguishes it from an astroblast.

From its histological appearances the tumour might justifiably be called a unipolar spongioblastoma. This name, however, has been given to a different kind of glioma that is composed of interlacing bundles of very long fibrillated uni- and bipolar cells, the processes of which are not directed towards vessels. The tumour reported in Case 1 is composed of a simpler and more primitive type of spongioblast than those found in the so-called spongioblastoma unipolare, and it is undoubtedly of a higher order of malignancy. The growth, therefore, cannot be called by any of the names used in Bailey and Cushing's classification, and for the present we do not propose to invent a name for it.

The case shows how previous beliefs about the occurrence of spinal metastases in cerebral gliomas may lead the observer astray in arriving at the correct localization of the primary tumour. The presence of severe pain in the right lower limb, of rigidity of the lower part of the spinal column, and of yellow spinal fluid of high protein content, indicated that there was a spinal tumour, presumably metastatic. This

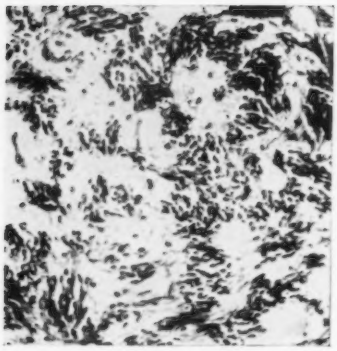

FIG. 1.

FIG. 2.

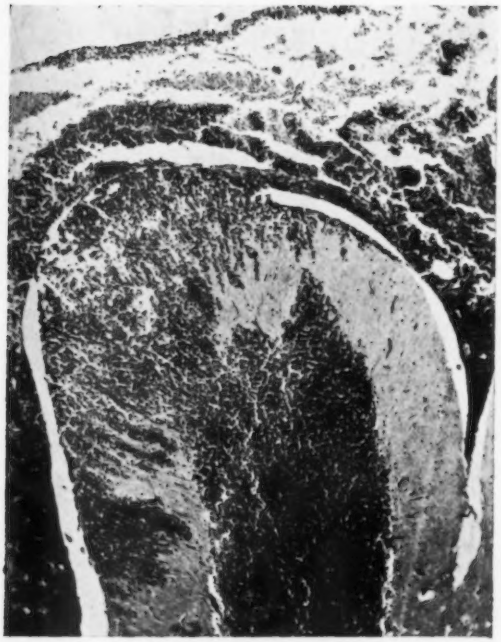

FIG. 4.

FIG. 6.

FIG. 1 (*Case* 1).—Primary tumour showing bundles of cells. Phosphotungstic acid hæmatoxylin. × 127.

FIG. 2 (*Case* 1).—Tumour in leptomeninges showing fibrillated unipolar cells with processes directed towards vessels. Phosphotungstic acid hæmatoxylin. × 222.

FIG. 4 (*Case* 2).—Invasion of folium of cerebellum by tumour cells from adjacent leptomeninges. Phosphotungstic acid hæmatoxylin. × 75.

FIG. 6 (*Case* 3).—Posterior surface of lower portion of spinal cord showing metastatic nodule on third lumbar segment.

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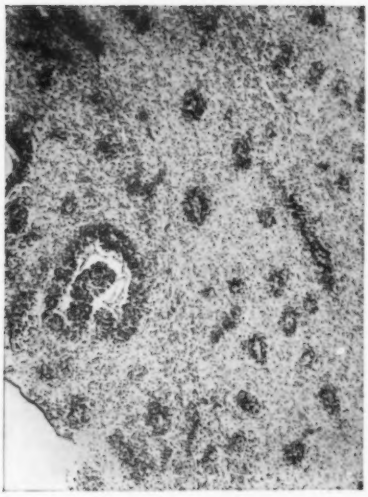

FIG. 7.

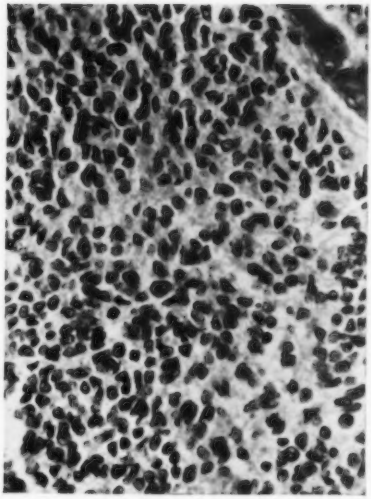

FIG. 8.

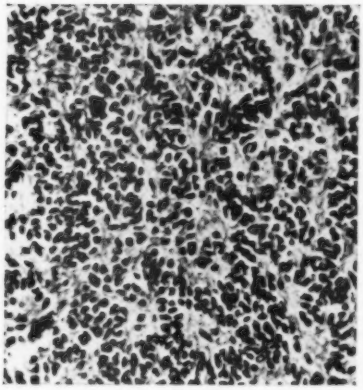

FIG. 10.

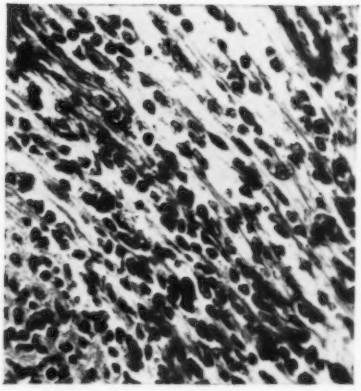

FIG. 11.

FIG. 7 (*Case* 3).—Wall of left lateral ventricle showing infiltration. Hæmatoxylin and eosin. × 42.

FIG. 8 (*Case* 4).—Medulloblastoma. The primary tumour. Hæmatoxylin and eosin. × 263.

FIG. 10 (*Case* 5).—Medulloblastoma. Primary tumour showing general arrangement of cells. Phosphotungstic acid hæmatoxylin. × 195.

FIG. 11 (*Case* 5).—Primary tumour showing fibrillated spindle cells. Phosphotungstic acid hæmatoxylin. × 380.

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FIG. 12.

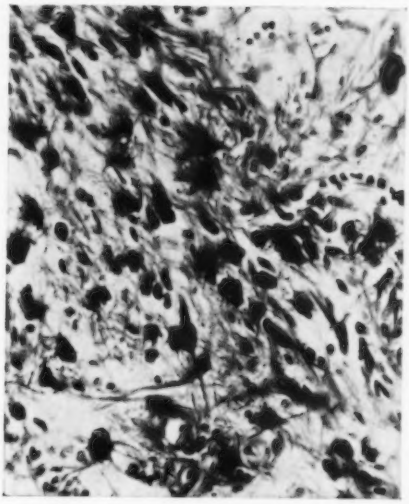

FIG. 14.

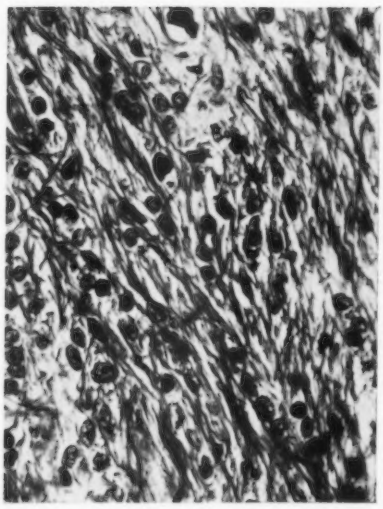

FIG. 15.

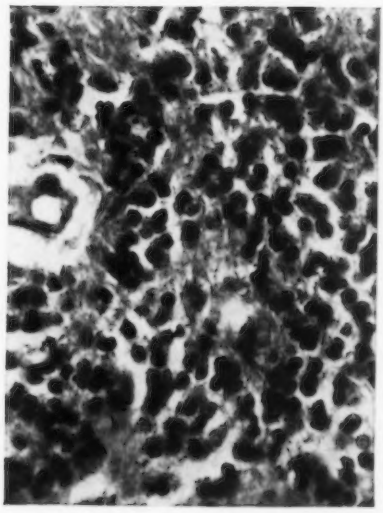

FIG. 16.

FIG. 12 (*Case* 6).—Glioblastoma multiforme. Tumour in genu of corpus callosum. Spindle cells with abundantly fibrillated cytoplasm are seen. Phosphotungstic acid hæmatoxylin. × 300.

FIG. 14 (*Case* 6).—Metastatic nodule attached to root in cauda equina. Numerous astrocytes and a few bipolar cells are demonstrated. Silver carbonate method for astrocytes. × 300.

Fig. 15 (*Case* 8).—Ependymoma. Primary tumour showing fibrillar area. The cells are elongated and contain numerous neuroglial fibrils. In several places blepharoplasten are seen in the cytoplasm close to the nucleus. Phosphotungstic acid hæmatoxylin. × 281.

FIG. 16 (*Case* 8).—Ependymoma. Primary tumour showing cellular area. The cells have a tendency to arrange themselves in groups round a central lumen. Phosphotungstic acid hæmatoxylin. × 281.

To illustrate paper by Hugh Cairns and Dorothy S. Russell.

was regarded as evidence in favour of cerebellar medulloblastoma, the only variety of glioma, with the exception of glioma of the retina, that has hitherto been recognized as a common source of metastases in the spinal subarachnoid space. Thus, in the presence of signs highly suggestive of a lesion of the third ventricle, we were led to explore first the cerebellum. It is remarkable that such extensive spinal metastases should produce such slight sensory and motor changes in the lower limbs.

This case clearly indicated the desirability of routine examination of the spinal cord at necropsy in all cases of cerebral glioma, and further examples of unsuspected spinal metastases were soon disclosed. The case reports that follow show that spinal metastases are not limited to the very malignant types of glioma, but may occur in almost all varieties.

NEURO-EPITHELIOMA.

Case 2.—*Glioma (neuro-epithelioma) of left eye. Enucleation of eyeball. Local recurrence, treated by radium. Massive invasion of central nervous system by tumour. Death.*

History: Arthur L., aged 3 years, was first admitted to the London Hospital under Mr. Goulden, on November 4, 1929, with the history that his mother had noticed one week before that his left eye was red and watery. The child had also suffered for some time from difficulty in breathing through the nose and from nasal discharge.

Examination: The lids of the left eye were swollen and there was considerable conjunctival and ciliary injection. The cornea was very cloudy though not ulcerated, and it had no reflex. The anterior chamber was partially filled with exudate and the iris was discoloured. The tension of the eye was normal. The child was rather drowsy, but general examination showed no other signs.

For one month the eye was treated with atropine and baths. The condition failed to improve and chemosis of the conjunctiva gradually developed. Therefore, on December 5, 1929, the left eye was excised.

Macroscopic Examination.

(Report of naked-eye appearances and histological preparations kindly provided by Mr. H. B. Stallard, of the Royal Ophthalmic Hospital, Moorfields.) The circumcorneal blood-vessels were injected. There was a hypopyon and the filtration angle of the anterior chamber was occluded by peripheral synechiæ. The lens was swollen and vacuolated. A yellowish white tumour with granular surface and soft friable consistency appeared to arise from the retina, which was almost entirely destroyed, and extended into the vitreous chamber. The choroid and optic disc were infiltrated and fragments of the tumour lay among the ciliary processes. There were several small areas which gave a gritty

sensation when the eye was divided. There was no macroscopic evidence of extra-ocular extension. The specimen was fixed in Zenker's fluid. After vertical division the globe was decalcified and embedded in celloidin.

Microscopic Examination.

In a median antero-posterior section, stained by hæmatoxylin and eosin, the posterior chamber is occupied by closely packed masses of tumour cells, which do not appear to be arranged in any special manner. Most of them are in various stages of degeneration and there are large anastomosing areas of necrosis, many of which contain neutrophil leucocytes. In the borders of such areas are occasional small deposits of amorphous, deeply hæmatoxyphil substance suggestive of calcium. The whole of the retina is replaced by tumour. Along one side of the globe the choroid is replaced at intervals by tumour cells and, on the same side, there is infiltration of the anterior layer of the iris and the lateral angle of the anterior chamber by tumour. The anterior chamber is filled with degenerating tumour cells and neutrophil leucocytes. The peripheral parts of the retina, which are not connected with the main mass in the posterior chamber, alone show a conspicuous arrangement of the tumour cells in rosettes of Flexner. These rosettes are hollow spheres, as can be seen in thicker parts of the section. In thinner parts they appear as a ring of cells, the nuclei of which lie at variable distances from the lumen. The nuclei are round, oval or pyriform; the narrow end of the pyriform examples is directed towards the lumen. They have a thick deeply-stained nuclear membrane and a thinner chromatin net beset with many fine dust-like nodes. There are no nucleoli. There is no demonstrable cytoplasm on the side of the nucleus remote from the lumen, but on the side towards the lumen there is a lightly eosinophil extension which ends in a more deeply eosinophil membrane. This membrane is slightly fuchsinophil when stained with van Gieson's mixture and appears pinkish-purple or purple in Mallory's phosphotungstic acid hæmatoxylin. Adjacent to the membrane on either side is a variable number of minute particles of inconstant size with similar staining properties, and occasionally small rounded bosses are seen that appear to be cytoplasmic protrusions beyond the membrane into the lumen. The lumen itself is frequently occupied by free tumour cells or by spheres that appear to be cytoplasmic detritus. There is no evidence of either cilia or blepharoplasten in the cells. Mitotic figures are very frequent.

Subsequent course: The child was discharged from hospital on December 15, 1929. In the following April he became irritable and swelling of the left eyelids recurred. In May it was found that there was a firm mass filling the whole of the left orbit and displacing the conjunctiva forwards. This was treated for six days by radon seeds and radium needles (total dosage, 1,728 millicurie hours). The eyelids became very swollen and sloughs discharged from the socket. In June, 1930, the child developed rubella and scarlet fever and was sent to an infirmary. He was admitted to the London Hospital once more in August in a wasted condition and suffering from loss of appetite.

There was now a large, irregular, firm red mass of tumour projecting forwards between the left eyelids, and from it came an offensive purulent discharge. On August 28, 1930, radium needles and radon seeds were again inserted into the tumour mass (12 mc. radium for five days, 6 mc. radon left *in situ*). There was severe vomiting for forty-eight hours. His condition then improved for a short time but he was still drowsy, and in the middle of September he became lethargic and began to vomit. Weakness of the right side of the face, increased tendon-jerks on the right side, and an extensor plantar reflex on both sides were observed. Two weeks later a projection of the right retina appeared below and to the outer side of the right optic disc, suggesting the presence of tumour behind. Vision of the right eye gradually failed, and in November the eye began to project forwards and its cornea became hazy. Vomiting occurred frequently, and the child became greatly wasted and finally died on November 28, 1930, almost twelve months after the primary tumour had been removed.

Summary of Necropsy. (*P.M.* 522, 1930.)

Marasmus. Gliomatosis of ventricles and of leptomeninges of brain and spinal cord. Primary glioma of left retina. Old operation: excision of left eyeball. Clear fluid in both middle ears. Slight œdema of myocardium. Atheroma of aortic cusp of mitral valve. Slight congestion and considerable emphysema of lungs. Œdema and considerable congestion of liver, spleen and kidneys. Congestion and mucous catarrh of stomach. Greatly wasted child.

Macroscopic Examination.

Orbits.—The left eyelids were glued together by a glistening brown membrane. In the centre of the left orbit there was a conical abscess cavity (1·8 by 0·7 cm.), the apex of which was directed backwards. It contained four radon seeds and thick brownish yellow pus. Its walls were composed of firm greyish white tissue, in some parts stained an orange colour. There was to the naked eye no evidence of tumour in the soft tissues of the right orbit, either in the orbital part of the optic nerve or in the right eyeball.

Brain.—The leptomeninges at the base of the brain were everywhere occupied by a milky-white deposit of finely granular appearance, which contained flattened areas (0·1 to 0·2 cm. in diameter) of greater opacity. This infiltration was most evident on the inferior surface of the cerebellum, in the cisterna basalis, on the orbital surface of the right frontal lobe, and on the inferior surfaces of both temporal lobes. In these places the sulci were conspicuously infiltrated with white deposits. The infiltration extended on to the superior surface of the cerebellum, the opposing surfaces of the great longitudinal fissure, and also on the convexities of the cerebral hemispheres in the form of discrete miliary deposits (0·1 cm. in diameter).

The optic chiasm and left optic nerve were replaced by a rounded, soft, friable greyish yellow mass (2·3 by 2·5 by 2·5 cm.). The proximal part of the right optic nerve (0·8 cm. in diameter) was also thickened by greyish white infiltration. The proximal parts of the third and sixth cranial nerves on each

side were occupied by greyish white nodular masses (up to 0·7 cm. in diameter), and the remaining cranial nerves were all embedded in a continuous mass of similar tissue (2·3 by 1·5 by 1·0 cm.) on each side of the pons and medulla oblongata. The pons was laterally compressed by these masses.

The floor of the third ventricle was replaced by a flocculent mass of growth continuous with the mass in the chiasmal region. The tela choroidea was covered with a gelatinous grey sheet of opaque tumour tissue continuous with the tumour in the leptomeninges of the great transverse fissure. The walls of both lateral ventricles and the fourth ventricle and the lateral walls of the third ventricle were studded with glistening grey nodules (up to 0·3 cm. in diameter). The choroid plexuses of the lateral ventricles appeared to be normal, except that there were a few nodules of tumour on the right choroid plexus at the foramen of Monro. There was moderate internal hydrocephalus.

Spinal cord.—The spinal subarachnoid space was everywhere distended with tumour tissue (up to 2·3 from side to side and 1·8 cm. from before backwards), appearing on section as homogeneous glistening greyish white growth enclosing the spinal cord. In the lower thoracic region the pattern of grey and white matter was not greatly disturbed by infiltration, but in the second thoracic segment the cord appeared on section as a central small trifoliate area, the margins of which were greatly eroded by infiltration. At the level of exit of the first lumbar nerves the cord (0·7 by 0·5 cm.) appeared to be extensively infiltrated by tumour.

Microscopic Examination.

Orbital extensions.—In the longitudinal section of the soft tissues of the left orbit a chronic abscess occupies the anterior half of the mass. The abscess cavity has a broad marginal zone of necrotic tissue beyond which is a stout layer of collagen infiltrated with numerous plasma cells and other cells that appear to be degenerating tumour cells. Amongst these are intra- and extracellular masses of golden brown pigment which give a positive reaction for iron. The orbital muscles are bound to this dense wall of collagen. There is atrophy and degeneration of the muscle fibres. Immediately behind the abscess is a triangular mass of tumour cells, interspersed with stout strands of collagen and enclosed laterally by collagen. There are irregular areas of necrosis amongst these tumour cells.

In a longitudinal section of the right eye the tumour cells are present along the course of the ophthalmic artery in the optic nerve, and a few cells lie around the small blood-vessels in the superficial layer of nerve fibres in the optic cup. Tumour cells lie in the sheath of the optic nerve between the collagen and the nerve fibres. They extend peripherally as far as the choroidal coat. There is no evidence in the retina of a second primary tumour or of invasion by tumour.

Intracranial extensions.—The cells composing the intracranial extensions are small round cells of the same kind as those in the retinal tumour. They are clumped together without any suggestion of rosette formation. In sections

stained with phosphotungstic acid hæmatoxylin there is no suggestion of blepharoplasten or fibrils in the scanty cytoplasm of these cells. The rounded mass replacing the optic chiasm is composed of cells that are very loosely aggregated in the meshes of a poorly vascularized scanty stroma. Much of the tissue has crumbled away and been lost in the process of embedding. There is extensive degeneration and necrosis of the cells, but in the neighbourhood of the vessels they are better preserved.

The inner border of the collagen sheath surrounding the right optic nerve is densely infiltrated with tumour cells. The cells encroach inwards between the bundles of nerve fibres and also infiltrate the nerve bundles themselves, especially at the edge of the section. A small area in the centre of the optic nerve is free from tumour.

There is extensive infiltration of the cerebral and cerebellar leptomeninges with tumour cells without apparent increase of reticulum. The cells also invade the cortex by way of the perforating vessels, forming stout cuffs both in the perivascular sheath and outside the sheath in the brain substance. A few rounded masses of tumour cells are also present in the cortex without any apparent relation to blood-vessels. This appearance may be the result of tangential section of perivascular masses. In the cerebellum columns of invading cells are seen in the molecular layer (fig. 4) which expand in a flask-like fashion on reaching the granular layer to extend around and deep to the Purkinje cells.

In the roof of the left lateral ventricle there is a thick irregular subependymal zone of closely packed tumour cells. The ependyma is raised into bosses by this infiltration and is missing at many points on their convexities. In a few places there is no subependymal infiltration. The tissue is moderately vascular and there are relatively few islands of necrosis. Reticulum is confined to the vessels.

Spinal extensions.—There is enormous distension of the subarachnoid space by densely packed tumour cells, especially in the lower thoracic cord. The blood-supply of these cells is scanty, and foci of degeneration and necrosis are conspicuous. The cells surround and invade the nerve roots, and there is extensive invasion and destruction of the cord itself in the form of large bays that encroach on the white matter. There is also, besides this direct extension inwards, a conspicuous infiltration of the perivascular spaces of the perforating arterioles forming thick cuffs. The cells are also present to a less extent in sleeves outside the pial invagination around these vessels. They are indistinguishable from the cells of the primary retinal tumour. There is severe degeneration of the anterior horn cells with much loss of Nissl substance and disappearance of their nuclei.

Comment.—In this case there was a primary tumour of the left retina which recurred in the left orbit after removal of the eyeball and spread profusely to the optic chiasm and right optic nerve and to the leptomeninges of the brain and cord. It invaded the floor of the third

ventricle and extended on the walls of all the ventricles. It also spread into the ventricles by way of the great transverse fissure and tela choroidea. The presence of well-developed rosettes of Flexner [11] in the primary tumour identifies it as a neuro-epithelioma of the retina, as defined and described by that author. The histological appearances agree closely with those described in his case. In our case the tumour cells infiltrating the brain, cord and leptomeninges did not form rosettes and were indistinguishable from medulloblasts.

In their structure, their high degree of malignancy and method of spread gliomas of the retina are very similar to medulloblastomas of the vermis and they are probably closely allied tumours. It has been suggested that the presence of rosettes in glioma of the retina betokens a lessened degree of malignancy as compared with tumours in which such formations are absent. The malignancy of this case, in which rosettes were present, was of such degree that it is doubtful whether this contention is correct.

Medulloblastoma.

Case 3.—Glioma (medulloblastoma) of cerebellum. Partial removal by operation. X-ray treatment. Temporary improvement. Sudden death after interstitial radon treatment.

History: R.H., a boot maker, aged 19 years, was admitted to the London Hospital on August 2, 1928, under the care of Dr. Cecil Wall. Apart from illnesses in childhood, he had been perfectly well until three months before admission, when he began to "talk through his nose" and to suffer from a heavy feeling in the head. The trouble with talking gradually increased, so that he had to pause for breath after each word. He was at first treated for nasal catarrh and deviation of the nasal septum, but four weeks before admission he began in the afternoons to have attacks of giddiness, followed by frontal headache and vomiting. In the attacks he had a sensation of falling backwards, and he would stagger and occasionally fall. At other times his gait was steady. The headaches became worse, so that one week before admission he could no longer work. He began to suffer from weakness of the right hand, and this was followed by occasional attacks of numbness of the right upper limb which lasted half an hour. From the onset of the illness he had occasionally seen distant objects as double, but his sight was not otherwise affected until a few days before admission, when it became dim during an attack of headache, and he saw lights and stars.

His speech became so bad that people could not understand what he was saying, and finally, after an intense attack of headache and vomiting, he passed into a state of stupor. On the following day he rallied partially and was then brought to the London Hospital. A lumbar puncture was done on the day of admission and 15 c.c. of clear cerebrospinal fluid, under greatly increased

tension, were withdrawn (protein, 0·017 per cent.; no white cells). Subsequently he was given rectal infusions of magnesium sulphate. For a week after admission he felt much better, though he continued to have occasional attacks of headache and vomiting. Later, the attacks of headache became very severe and extended to the back of the neck. In addition, he began to have pain in the right side of the face. He was transferred to the surgical wards on August 11, 1928. At no time during the illness was there any difficulty in swallowing or regurgitation of fluids through the nose.

Examination: The patient was in great pain and was at times drowsy. He yawned frequently. The other positive findings were pronounced dysarthria; generalized tenderness of the skull, greatest in the suboccipital region, and of the back of the neck; bilateral papilloedema (2·5 diopters); venous engorgement and swelling of upper eyelids; bilateral ptosis; weakness of right external rectus; slight weakness of lower part of face on the left side; occasional relative deafness of right ear; generalized hypotonia; slight dysmetria, ataxia and dysdiadokokinesis of all four limbs; diminution of all tendon-jerks, especially the knee-jerks; slight enlargement of the sella turcica and erosion of the clinoid processes. No objective changes were found to correspond with the numbness of the right arm and the pain in the right side of the face. Examination of the tongue and palate showed no defect of movement, and fluids were swallowed without any trouble. There was no nystagmus. During the three days before operation the pulse-rate slowed from 70 to 46, and the respirations became slow, periodic and sighing in character.

Operation, August 14, 1928: Under local anæsthesia, with the addition of morphia, $\frac{1}{6}$ gr., the cerebellum was exposed by the usual crossbow incision. When the dura was opened the cerebellum bulged greatly, in spite of the fact that the intracranial tension had been previously reduced by tapping the occipital horns of the lateral ventricles. Both tonsils were displaced through the foramen magnum, and the arch of the atlas was therefore removed. The tonsils were widely separated, but no tumour was found in the region of the medulla or calamus scriptorius. A median vertical incision was now made in the vermis, and at a depth of 4 cm. an ill-defined, soft, grey tumour was encountered, high up under the tentorium. After fragments had been removed for section (S.D. 1940, 1928), the tumour was sucked out, but, owing to the condition of the patient and the fact that the tumour was in a relatively inaccessible part of the vermis, removal was not complete.

Post-operative course.—After operation there was complete relief from headache, vomiting and vertigo, and articulation improved. Papilloedema subsided and visual acuity was $\frac{6}{9}$ in each eye. On discharge from hospital thirty-one days after operation he could walk unaided, but his gait was still ataxic. He returned to work.

X-ray treatment was begun by Dr. Vilvandré in September, 1928, but the patient was not regular in attendance for treatments. In February, 1929, he began to suffer once more from headache, and his walking and the movements of his left hand became more unsteady. After each X-ray treatment he

experienced temporary relief, but ataxia of the left hand steadily increased and prevented him from working. In June, 1929, the relief after X-rays was much less than it had been earlier in the year. On July 17, 1929, he was re-admitted to hospital for radium treatment. He was at this time drowsy, irritable, and incontinent of urine and fæces. Papillœdema had recurred (4·5 D.) with the formation of retinal hæmorrhages, and visual acuity had diminished. There was left hemiparesis of moderate degree and almost complete right facial paralysis. A careful examination was made for clinical evidence of spinal metastases, but beyond doubtful analgesia up to the sixth thoracic segmental level on the right side there was nothing that could be clearly attributed to a lesion of the spinal cord. On July 18, radon seeds containing 11 millicuries were inserted into the tumour in the region of cerebellar vermis by trocar and cannula. Two hours later the patient suddenly stopped breathing and died.

Summary of Necropsy. (*P.M.* 275, 1929.)

Hæmorrhage into glioma (medulloblastoma) of cerebellum. Operation: old cerebellar decompression; recent insertion of radon. Bilateral focal fibrous pleurisy. No tuberculous nodules in lungs or in bronchial lymph glands. Healed appendicitis; fibrous stricture with fibrosis and muscular hypertrophy of appendix. Uniform colloidal hypertrophy of thyroid gland. Congestion of liver, kidneys, and mucosa of stomach. Foramen ovale patent. Very slight atheroma of descending thoracic and abdominal aorta, and of bifurcation of carotid arteries. Polypous adenoma (0·6 cm. in diameter) in pelvic colon. Meckel's diverticulum (4·5 by 1·6 cm.) situated 106 cm. above cæcum. A wasted lad.

Macroscopic Examination.

Brain.— The brain was fixed *in situ* nineteen hours after death. A very large tumour (8·0 by 7·5 by 4·5 cm.) occupied the greater part of the cerebellum. In its posterior part about 2 to 3 drm. of blood-clot surrounded radon seeds. This hæmorrhage presumably followed the insertion of radon and was the immediate cause of death. Apart from the area of hæmorrhage the cut surface of the tumour was soft, pinkish white and faintly granular. The tumour involved the upper surface of the vermis and left lateral cerebellar lobe, and the roof of the fourth ventricle. It extended more to the left than the right and invaded the tentorium on the left. On each side the anterior surface of the lateral cerebellar lobe was displaced into the internal auditory meatus. The pons and medulla oblongata were flattened against the basi-sphenoid and basi-occiput. The upper part of the pons was displaced to the right, while the lower part of the medulla oblongata and the adjacent cervical spine were displaced to the left.

The aqueduct of Sylvius was dilated (0·35 cm. in diameter). The third ventricle, however, was not dilated; its walls were thrown into folds by a layer of tumour tissue, its floor was slightly thickened (0·15 cm.), and anteriorly its

right lateral wall presented a nodule of tumour (1·5 by 1·0 cm.) which projected up to 0·4 cm. into the lumen of the ventricle (fig. 5). Both lateral ventricles were small and appeared everywhere to be lined with tumour tissue, which in some places produced longitudinal corrugations and in others nodular projections (up to 0·8 cm. in diameter) (fig. 5). In places the tumour lining the ventricles had invaded the adjacent brain; the fornix was almost completely replaced by grey granular growth, and the lower surface of the corpus

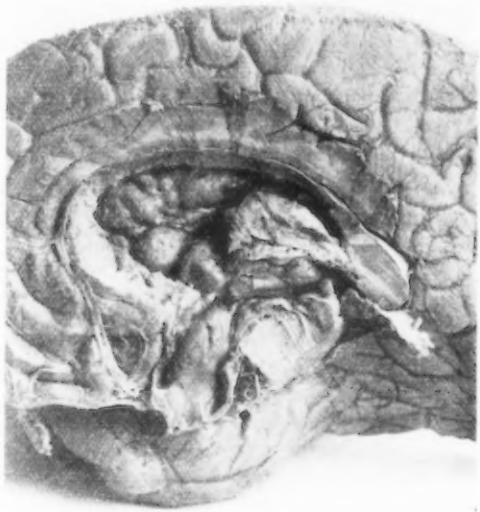

FIG. 5 (*Case* 3).—Right lateral and third ventricles with corpus callosum cut away to show growth in their walls.

callosum was invaded to a depth of 0·7 cm. The left hippocampal gyrus contained an extension of tumour from the left temporal horn that measured 2·6 by 1·8 cm. The anterior part of the pineal gland (0·8 by 0·6 cm. in sagittal section) was replaced by a nodule of granular white tumour (0·5 by 0·3 cm.). The surfaces of the cerebral hemispheres appeared to be free from metastases.

Spinal cord.—There was a brownish white hemispherical nodule (0·6 cm. in diameter) on the right side of the posterior surface of the third lumbar segment (fig. 6). On the arachnoid over the posterior surface of the fourth thoracic segment there was a small grey nodule (0·2 cm. in diameter). Elsewhere the cord and its membranes appeared to be free of metastases.

Microscopic Examination.

The primary tumour.—The borders of the tumour in the cerebellum are ill-defined and the neighbouring cerebellar folia, the roof of the fourth ventricle

and tentorium cerebelli are invaded by the growth. The tumour is of a richly cellular nature. The cells are closely packed together, especially about the blood-vessels. In parts distant from the vessels there are often small poorly-defined areas of degeneration and necrosis which are sometimes occupied by collections of neutrophil leucocytes. There are also small irregular cystic spaces containing rounded masses of homogeneous eosinophil substance. In the tentorium the tumour cells often lie in parallel rows between collagen strands or in rounded masses, the centres of which are less densely cellular than the periphery.

The individual cells have round or oval nuclei with a deeply-stained fairly thick nuclear membrane and a fine chromatin net beset with a few nodes of variable size. There are one or two conspicuous nucleoli in the majority of the nuclei. The cytoplasm is eosinophil and very scanty; it appears fluffy and is not prolonged into definite processes. In preparations stained with phosphotungstic acid hæmatoxylin there is no evidence of fibrils or of blepharoplasten. The cells are refractory to the gold chloride sublimate method of Cajal.

The cerebral extensions.—The walls of the third and lateral ventricles, including the ventral part of the fornix, are diffusely infiltrated with cells of the same kind as those in the primary tumour (fig. 7). The cells are chiefly collected in dense zones beneath the ependyma and round the blood-vessels in the deeper tissues. In the third ventricle the infiltration extends down to and involves the leptomeninges covering the floor. The ependyma is intact in some places and in many others is replaced by masses of tumour cells. In the descending horn of the left lateral ventricle fissures lead from the cavity into the adjacent infiltrated tissue. There is considerable degeneration of the cells that are remote from blood-vessels and numerous fat granule cells lie amongst them. The majority of blood-vessels that are surrounded by tumour cells appear normal, but in others the walls are thickened by an increase in the number of endothelial cells, and in certain of these the endothelial cells appear to be mixed with tumour cells which have spread inwards by direct extension across the perivascular space. The infiltration is especially dense in the left hippocampal gyrus, and in one part the tumour cells extend outwards as far as the surface of the brain, occasionally breaking through into the leptomeninges. The anterior half of the pineal body is densely infiltrated with tumour cells, but the rest of the gland appears normal. There is no evidence of tumour in the leptomeninges of other parts of the cerebral hemispheres, or in the portions of the optic tract examined.

The spinal metastases.—The fifth cervical segment is free from tumour. The left dorsal root of the fourth thoracic segment and both dorsal roots of the third lumbar segment are surrounded by a circumscribed lenticular mass of tumour cells occupying the subarachnoid space close to the exits of these roots from the spinal cord. Of these the mass on the right third lumbar root is the largest. The cells are arranged in round clumps or in columns along the collagen strands that form the stroma of these metastases. There is slight

invasion of the marginal glia of the cord by tumour cells at the medial extremity of the largest metastasis only.

The fundi.—There is papillœdema but no invasion by the tumour cells.

Comment.—This glioma is, histologically, a typical medulloblastoma. The ventricular method of spread in this instance offers a striking contrast to the distribution of metastases observed in the next case to be described. In this connection it is to be noted that when first disclosed at operation the tumour was limited to the upper part of the vermis and did not extend into the cisterna magna. This fact doubtless influenced the method of spread.

Case 4.—Glioma (medulloblastoma) of cerebellum invading pons and medulla oblongata. Numerous cerebral and spinal metastases. Cerebellar decompression and partial removal of tumour. Early fatality.

History: Bernard B., aged 5½, referred by Professor Ellis, was first seen on June 30, 1930. Six months before this he began to suffer from slight headaches and drowsiness, and a few weeks later from projectile vomiting, especially in the mornings. He rapidly lost weight and his legs gave way at times when he was walking. Five weeks before admission he seemed very weak and was confined to bed; and at this time also he began to have difficulty in micturition, which later changed to incontinence. On two occasions, about three weeks before admission, he appears to have had attacks of extensor rigidity. Attacks of coughing occurred frequently. He became increasingly languid, but the headaches were never severe and they disappeared completely one month before admission.

Examination: The boy was intelligent but irritable and lethargic, and was very wasted. His head was slightly enlarged (circumference 51·6 cm.) and there was spasm of the muscles of the right side of the back of the neck. There was also considerable hyperextension and rigidity of the neck. His face and trunk were persistently rotated towards the right and he strongly objected to being placed on his left side. Though his parents had not noticed anything wrong with his vision, the boy was almost blind; he could not count fingers beyond 2 ft. with his right eye and had perception of light only in the left eye. There was bilateral papillœdema (right, 4·5 D; left, 6 D) with secondary atrophy and perivascular exudate. The upper eyelids were engorged and both eyeballs were rather prominent. There was persistent conjugate deviation of the eyes to the right, together with almost complete loss of voluntary conjugate movement to the left. At the extremes of his lateral ocular movements there was coarse ill-sustained nystagmus. Upward movement of the right eye was slightly defective and there was ptosis on the right side. The corneal reflexes were diminished and there was lower facial weakness on the right side. When he was sat up in bed he had great increase of hyperextension of the head, his eyes became more prominent, and his abdominal muscles contracted as though he were going to vomit, but he did not actually do so. His pulse at this time did

not alter (rate 120). Movements of the left upper limb were weak and ataxic and there appeared to be relative astereognosis of the left hand. All the limbs were hypotonic, the left more than the right. All the tendon reflexes and the abdominal reflexes were absent, and the plantar reflexes were extensor. He was incontinent of urine and fæces and had frequent attacks of hiccough and of vomiting.

During the period of observation the boy gradually became dysarthric. Lumbar puncture had been done on June 26, 1930, because tuberculoma with tuberculous meningitis was suspected, and the 8 c.c. of fluid withdrawn contained 7 lymphocytes per cubic millimetre and 0·08 per cent. of protein. X-rays of the skull showed separation of the sutures and slight erosion of all the clinoid processes.

Diagnosis.—This case was considered to be most probably a medulloblastoma of the vermis, and it was regarded as particularly unfavourable because of the extent of involvement of the brain-stem, as indicated by the severe disturbance of lateral conjugate movement of the eyes and the obvious pyramidal signs. However, although the boy was practically blind, the condition of the fundi suggested that some sight might be regained if the lesion could be adequately dealt with, and operation was therefore decided upon, notwithstanding the child's poor condition and increasing drowsiness.

Operation, July 8, 1930: Intratracheal gas and oxygen. The cerebellum was exposed by the usual crossbow incision, after both lateral ventricles had been tapped and found to contain much fluid under greatly increased pressure (more than 650 mm. of cerebrospinal fluid). When the dura was opened the cisterna magna was seen to contain a soft red tongue of tumour which passed down through the foramen magnum to the lower border of the axis. It was necessary to remove the posterior arch of the atlas before this mass could be tilted out. The vermis was now divided in the middle line and the main part of the tumour was thus exposed. At its junction with the outgrowth into the cistern it was constricted by a vessel. The tumour was soft, and by means of suction about one-third of it was removed before the child's condition rendered it advisable to stop. After the usual closure a blood transfusion was given.

Post-operative course.—The child soon responded but was rather drowsy and he had frequent attacks of hiccoughs. Thirty hours after operation his temperature rose to 104·6°, breathing became jerky and irregular, and he died two hours later.

Summary of Necropsy. (*P.M.* 301, 1930.)

Metastatic glioma of leptomeninges of brain and spinal cord. Primary glioma (medulloblastoma) of vermis of cerebellum. Operation: subtentorial decompression and partial removal of tumour. Slight atheroma in mitral valve of heart. Mucous catarrh of stomach. Pink marrow in upper half of shaft and in neck of femur. Pallid, considerably wasted boy.

Macroscopic Examination.

Brain.—The brain was fixed fifteen hours after death. A partially excavated mass of soft pinkish white tumour (6 by 3 cm.) occupied the fourth ventricle and lower part of the vermis and extended into the dilated aqueduct of Sylvius (0·7 cm. in diameter). The tumour invaded the dorsal surface of the pons and medulla oblongata to a depth of 1·2 cm. From the left side of the medulla oblongata the tumour extended into the left cerebello-pontine angle. Here it formed a soft white mass (2·2 by 1·4 cm.) on the anterior surface of which ran the left lower cranial nerves. There was an isolated mass of tumour (1·0 by 0·6 cm.) in the highest point of the vermis. The surface of the cerebellum was completely covered by a semitranslucent white film of tumour tissue, which extended ventrally to cover the anterior surface of the pons. The film was thickest on the superior surface of the cerebellum, especially at its most anterior central part. On the inferior and anterior surfaces of the cerebellum there were also numerous, often confluent, opaque white plaques of tumour. Similar isolated plaques (up to 1·4 by 1·2 cm.) were seen on the surface of the right third frontal convolution, the right inferior temporal convolution and on the internal surface of each cerebral hemisphere.

The lateral ventricles were greatly dilated (capacity: right, 56 c.c.: left, 48 c.c.). The third ventricle was also dilated; its walls were everywhere smooth, except alongside the entrance of the aqueduct of Sylvius where there was a nodule of soft tumour tissue (0·2 cm. in diameter) continuous through the aqueduct with the main tumour. On the choroid plexus of the third ventricle were several soft white miliary deposits of tumour (0·2 by 0·1 cm.).

Spinal cord.—Below the eighth cervical segment the posterior surface of the cord was covered by a film of white granular tissue (up to 0·15 cm. thick) which frequently enveloped the posterior roots at their attachment to the cord. This film was attached to the cord but not to the overlying arachnoid, which itself showed numerous semitranslucent milky-white spots and confluent areas, especially in the region of the cauda equina.

Microscopic Examination.

The main tumour consists of a compact mass of cells (fig. 8) which have a small amount of very indefinite cytoplasm. The nuclei are rounded or oval and have a thick membrane and a fine chromatin net which is plentifully studded with nodes of varying size. The majority of nuclei contain from one to three small nucleoli. Multinucleate giant cells are present occasionally and mitotic figures are plentiful. With Mallory's phosphotungstic acid hæmatoxylin there is no evidence of neuroglia fibrils. The cells are refractory towards gold and do not show any further details of structure in silver preparations. In some areas the cells have each a fine short eosinophil process and tend to be arranged in the rosettes of Wright. In other places the cytoplasmic process is directed towards the wall of an adjacent blood-vessel. There is no reticulum apart from the walls of blood-vessels.

The tumour invades the adjacent cerebellum, the anterior corpora quadri-

gemina and the dorsal surface of the pons and medulla oblongata. The infiltration in the floor of the fourth ventricle extends downwards around the upper part of the central canal which, in the lower medulla oblongata, consists of a group of small canals lined with ependyma. The leptomeninges covering the mid-brain, the medulla and upper part of the vermis are densely infiltrated with growth and the invasion of the underlying tissue is both diffuse and perivascular in character. There is an increase of reticulum where the leptomeninges are infiltrated.

The cerebral metastases.—There are focal discrete areas of secondary growth in the leptomeninges of the cerebral hemispheres and over the floor of the third ventricle. In the larger of these the tumour cells spread downwards into the sulci, whence they invade the adjacent brain tissue both by direct extension and indirectly by infiltrating the perivascular sheaths of the perforating vessels. The cells lie both inside the sheaths and immediately outside in the brain substance. In a vessel near the floor of the third ventricle the cells are all outside the sheath. A small collection of tumour cells is situated at the base of the choroid plexus of the third ventricle, where it is suspended from the tela choroidea. The plexus itself, the adjacent fornix and the ependyma of the third ventricle are not affected.

The spinal metastases.—In a section through the twelfth thoracic segment there is diffuse infiltration of the subarachnoid space and of the subjacent pia over the dorsal and to a less extent over the lateral aspects of the cord. There also is a small collection of tumour cells at the opening of the ventral fissure. The superficial parts of the posterior columns are invaded from the pia, both by direct extension and by the growth of cells inwards around the perivascular spaces. The margin of the spinal cord is slightly crenated along the posterior border.

Comment.—The glioma described in this case is a medulloblastoma and exhibits the characteristic features of this type in its situation, its macroscopic and microscopic appearances and in the extensive distribution of metastatic deposits. The meningeal spread of this tumour affords an interesting comparison with Case 3, in which a massive intraventricular spread was demonstrated. In the case under discussion there was no ventricular spread anterior to the aqueduct of Sylvius, but the cells were distributed by the circulation of the fluid in the subarachnoid space. By this means they reached the base of the brain, the convexities of the cerebral hemispheres and the spinal cord. They also spread inwards by the velum interpositum to the attachment of the choroid plexus of the third ventricle.

The appearances at necropsy fully justified the misgivings that we had had about operating on this boy. The case was clearly a hopeless one, but in the present state of clinical knowledge it is not possible to refuse operation in a case of this type, especially when there is only

slight rise of protein in the cerebrospinal fluid, lest in so doing a benign type of glioma that responds well to surgical treatment, as for example a cystic astrocytoma of the vermis, should be occasionally overlooked. The main hope of treatment in this type of case, and in cases like Case 2, would seem to be in massive radiation of the whole nervous system.

Case 5.—Glioma (differentiating medulloblastoma) of cerebellum. Ventricular and spinal metastases. Unusually long history of illness. Subtemporal decompression. Death.

History: Ronald J., aged 9 years, referred by Professor Ellis, was first seen on November 13, 1930. For six years he had had frequent attacks of morning vomiting associated with anorexia and listlessness. However, he was able to attend school regularly until one year before admission, when he began to suffer from daily attacks of frontal headache and unsteadiness in walking. The headaches became increasingly severe. Six months before admission he was sent home from school because he could not see the blackboard, and within a short time he was unable to see to read. He began to dream and to talk in his sleep. One month before admission he complained of pain in the left thigh, and he became very tired.

He had always been slightly undersized and plump. All his life he had suffered from frequency of micturition when cold, and his mother said that for some time he had passed an abnormally large amount of urine.

Examination: The patient was a somewhat drowsy boy of slightly short stature and normal intelligence (weight, 23·2 kilogrammes; height, 1·22 metres). Pulse-rate, 66. His head was enlarged (circumference, 55·2 cm.), and there was tenderness in the suboccipital region, also pain on flexion of the neck. When standing, his head drooped towards the left shoulder. The left complexus muscle was rather prominent. Both optic discs showed papilloedema measuring 4 D., and on the right side there were streaks of bright yellowish white exudate converging from the edge of the disc towards the macula. Visual acuity: right, 0·5/18; left, 1/18. There was coarse nystagmus on lateral and upward movement of the eyes. Lateral conjugate movements of the eyes were considerably impaired, particularly to the left. He was very unsteady in walking and standing, tending to fall in any direction. There was no gross inco-ordination or weakness of his upper limbs. No tendon reflexes could be elicited. The abdominal reflexes were brisk and equal on the two sides, but the plantar reflexes were extensor. Postural sensibility was slightly impaired in the right big toe and there was relative astereognosis of the right hand. X-rays showed separation of the sutures and moderate enlargement of the sella turcica.

A diagnosis was made of tumour of the posterior fossa. The great disturbance of lateral conjugate movement of the eyes raised the question whether the tumour might not lie in front of rather than behind the floor of the fourth ventricle, but the long history was against this, and it was felt that we were most probably dealing with a slowly developing tumour of the vermis. On the eve of operation he had an attack of extensor rigidity of the limbs and

hyperextension of the head, and from his nostrils there was a profuse discharge of watery fluid (? cerebro-spinal rhinorrhœa).

Operation, November 11, 1930: A cerebellar exploration was planned, but as a preliminary measure both lateral ventricles were tapped to determine whether there was symmetrical hydrocephalus. Owing, as was subsequently proved, to misdirection of the ventricular needle, the right ventricle could not be found, whereas the left ventricle contained abundant fluid under a pressure of 550 mm. of cerebro-spinal fluid. This observation raised the possibility that the tumour might be in the right hemisphere, and we therefore decided to temporize by doing a right subtemporal decompression. This was a bad error of judgment, for the clinical signs pointed to a lesion of the posterior fossa.

Two days later, a few hours before a cerebellar exploration was to have been done, the boy suddenly stopped breathing and died, in spite of immediate tapping of the left ventricle.

Summary of Necropsy. (*P.M.* 510, 1930.)

Metastatic glioma of ventricles and spinal subarachnoid space. Primary glioma of vermis of cerebellum. Operation: ventricular estimation and right subtemporal decompression. Very slight atheroma of mitral valve and aortic commissure. Considerable injection of trachea. Congestion, œdema, slight peribronchial hæmorrhages and acid digestion of posterior parts of lungs. Congestion of kidneys and liver. Numerous cysts (up to 2·3 cm. in diameter) in cortex and medulla of kidneys. Petechial hæmorrhage in first part of duodenum. Slight injection of ascending colon. Cheesy concretions in crypts of tonsils. Nodule of cartilage (0·4 cm. in diameter) in spongiosa of upper part of shaft of right femur. Well developed, well nourished boy. The spleen was not examined as it was used for injection experiments.

Macroscopic Examination.

Brain.—The brain was removed twenty-four hours after death. A tumour (6·6 by 6·2 by 3·8 cm.) occupied almost the whole of the vermis of the cerebellum (fig. 9) and presented on the posterior surface between the lateral lobes, and also immediately below the left choroid plexus of the fourth ventricle, where it formed a spherical nodule in contact with the left vagus and spinal accessory nerves and the adjacent left restiform body. The tumour was composed of soft, faintly granular, white tissue, in which were numerous small areas of hæmorrhage (0·1 cm. in diameter). In its centre there was a cavity (1 cm. in diameter) lined with blood-clot. The tumour was in most places sharply defined from the surrounding cerebellum, but it was attached to the lower part of the floor of the fourth ventricle. The upper part of the fourth ventricle was still patent and contained a nodular outgrowth from the main tumour which extended almost to the posterior end of the greatly dilated and shortened aqueduct of Sylvius (length 0·6 cm.; diameter 1·4 cm.). The pons and medulla oblongata were greatly flattened and displaced forwards, and each olive showed a groove where it was in contact with the corresponding vertebral artery.

There was severe internal hydrocephalus. The third and lateral ventricles were greatly dilated. The potential space of the fifth ventricle had been opened up by separation of the layers of the septum lucidum. This space connected with the lateral ventricles by rounded holes in each layer of the septum lucidum (fig. 9). All the convolutions were broad and the intervening sulci shallow. The tonsils of the cerebellum projected downwards a short distance through the foramen magnum, and there was great downward projection of each frontal lobe on to the cribriform plate of the ethmoid. No opening was found in the dura at this region.

FIG. 9 (*Case* 5).—Right half of brain showing large primary glioma of cerebellum, and a metastatic nodule on the anterior wall of the dilated third ventricle. Immediately in front of the foramen of Monro the septum lucidum shows a large perforation.

Several other tumours, smaller than the primary tumour, were found in the ventricular system. On the anterior wall of the third ventricle there was a tumour (1·2 cm. in diameter) which filled the optic and infundibular recesses and surmounted the optic chiasm (fig. 9). On the floor of the anterior horn of the right lateral ventricle there was a plaque of tumour tissue (0·9 by 0·9 by 0·3 cm.). Two nodules were found on the walls of the left lateral ventricle, one (0·3 cm. in diameter) on the floor of the anterior horn, the other (0·5 cm. in diameter) on the posterior wall of the descending horn.

Spinal cord.—The arachnoid covering the posterior surface of the lower thoracic part of the spinal cord showed numerous opaque, greyish-white spots, about 0·1 cm. in diameter. On the anterior root of the fourth lumbar nerve on the right side, about 1 cm. below the level of the conus medullaris, there was a small grey nodule (0·25 cm. in diameter). The adjacent fifth lumbar anterior root was lightly adherent to this nodule.

Microscopic Examination.

The primary tumour.—The tumour is uniformly of a densely cellular character (fig. 10). These cells in general are small and possess scanty cytoplasm and oval or rounded nuclei. The nuclear membrane is stout and the chromatin net is of a close mesh and plentifully studded with deeply-stained nodes. There are from one to three nucleoli in most of the nuclei. The cytoplasm is eosinophil. It tends to be drawn out into short poorly-defined processes from one or both poles of the nucleus when the nucleus is elongated, and forms an indefinite fluffy zone when the nucleus is more spherical. A few multinucleate giant cells and occasional mitoses are present. There are no blepharoplasten. The architecture of the tumour varies with gradual transitions from one area to another. In some places the cells are closely clustered together with no architectural relationship to one another. In other places there is an evident formation into the rosettes of Wright. These are most conspicuously developed near the roof of the fourth ventricle. Frequently the rosettes are incomplete and the cells then appear in undulating palisades. More rarely the delicate non-fibrillated cytoplasmic processes of the cells radiate towards vessels, but without any attempt to form expansions where they terminate. In still other areas the cells are definitely of spindle form and lie together in bundles. In many of these cells there are fine sharply stained neuroglial fibrils in sections, stained by phosphotungstic acid hæmatoxylin (fig. 11). Apart from these intracellular fibrils there are in parts of the tumour other stouter neuroglial fibrils that run between the cells and appear to belong to certain large fibrillary astrocytes. These astrocytes are interpreted as belonging to the original cerebellar tissue that has suffered invasion by the tumour, since they are principally found near the edge of the tumour and there are no demonstrable transition forms between them and the tumour cells proper. They have an affinity for gold when treated by Cajal's method. The reticulum in the tumour is limited to the walls of the blood-vessels and the leptomeninges.

The invasive character of the tumour is demonstrated by a tongue-like process that extends into the fourth ventricle and is adherent in places to the floor of the ventricle. Beneath such areas the pons and medulla oblongata are also infiltrated with tumour cells. There is slight infiltration of the choroid plexus of the fourth ventricle at its point of attachment. The cerebellum is conspicuously infiltrated: the tumour reaches the leptomeninges at the posterior border of the vermis and extends to the depths of the sulci along the dorsal border in the mid-line.

The cerebral metastases.—The nodules in the third and lateral ventricles are all of similar appearance, and closely resemble the cerebellar tumour in their cytology. They occupy the subependymal tissue. The ependyma is reflected upwards at the borders of the nodules but is missing over their convexities. Near the larger nodules there are occasional microscopic deposits of tumour cells beneath the ependyma; in such places the ependyma is not raised but shows a small break in continuity. This suggests that the tumour cells gain entry to the subependymal tissues through a rupture in the ependyma.

Such a process would doubtless be facilitated by internal hydrocephalus. The nodules are fairly discrete and the tumour cells do not invade the underlying tissues deeply. Thus, the cells forming the mass in the floor of the third ventricle do not extend to the leptomeninges at the base. A considerable number of giant cells and mitotic figures is present. There is less variety of cell type and arrangement than in the primary tumour; fibrillated spindle cells are absent and the tendency to form the rosettes of Wright is less marked on the whole. The majority of the cells are of the simplest form with a scanty cytoplasm that is drawn out into a short process at one point (pyriform cells). There is no reticulum save in the leptomeninges and in walls of blood-vessels.

The spinal metastases.—In the transverse section of the twelfth thoracic segment the subarachnoid space and the pia over the posterior columns are infiltrated somewhat scantily with tumour cells of round or pyriform type. The cells are slightly more abundant about the blood-vessels than elsewhere. There is no invasion of the substance of the cord by tumour.

The nodule on the anterior root of the fourth lumbar segment is composed of a discrete mass of round or pyriform tumour cells that surround the root and penetrate between the individual nerve-fibres, forming rows and small clusters. These cells are identical with the cells seen in the primary tumour and in the ventricular metastases.

Comment.—Most of the cells in the primary cerebellar tumour are medulloblasts, and the tumour must therefore be regarded as a medulloblastoma (fig. 10). The arrangement in rosettes of Wright in many places is characteristic of medulloblastoma, although not confined to this type of glioma. In some areas of the tumour spongioblasts with fibrillated processes (fig. 11) are so numerous as to indicate a degree of differentiation unusual in cerebellar medulloblastoma, though not unusual in medulloblastoma of the cerebrum (Cushing [7]). The metastases in this case emphasize the primitive character of the tumour, and have the cytological appearances of a typical medulloblastoma. The discrete character of the cerebral metastases is perhaps correlated with an unusually low grade of malignancy for this kind of glioma and provides a very striking contrast with the ventricular method of spread in Case 3.

The metastatic nodule in the floor of the third ventricle was possibly responsible for the persistent polyuria, in which case it can be inferred that metastasis occurred at a considerable interval of time before the death of the patient. The relatively slow growth of the tumour is doubtless to be correlated with the conspicuous tendency towards histological differentiation. Six years history of illness is most unusual in a case of cerebellar medulloblastoma.

Glioblastoma Multiforme.

Case 6. *Glioma (glioblastoma multiforme) of left frontal lobe and corpus callosum. Death six weeks after onset of symptoms.*

History: William A., an engine driver, aged 56, was admitted to the London Hospital under the care of Dr. Riddoch on August 14, 1930, in a semiconscious condition. He had always been healthy and, apart from depression following the death of his wife in October, 1929, had remained well until five weeks before admission, when he began to lose interest and to show signs of disorientation and impairment of comprehension. He continued at work for a further two weeks, but towards the end of that time was observed by his fireman to be in a dazed condition while driving his engine. Three weeks before admission he began to have severe headache in the occipital region extending down to the neck, and he complained of a noise in his head like the noise of an electric train. Micturition became difficult. He took to his bed, but the headaches grew worse for a week and he became more and more drowsy. His speech, which had hitherto been normal, became monosyllabic, slurred and wandering. For one week before admission he was unable to feed himself and was at times incontinent of urine.

Examination: On admission the patient was in a semicomatose condition. Temperature, 98·6° F. Pulse-rate, 110. Respirations were of Cheyne-Stokes character and his face and extremities were cyanosed. He was incontinent of urine and fæces. He resented passive movements of his head and his neck was rigid. There was slight bilateral papilloedema, more marked on the left side. The pupils were dilated and fixed. The right side of the face was paralysed and there was considerable weakness of the right upper and lower limbs. The abdominal reflexes were absent. Kernig's sign was present.

Lumbar puncture on the day of admission yielded 8 c.c. of slightly yellow fluid which formed a fine cobweb: 31 white cells per cubic millimetre (polymorphonuclear neutrophils 40 cent., lymphocytes 60 per cent.): protein, 0·5 per cent.; Wassermann reaction, negative.

The patient developed retention of urine and became progressively more deeply unconscious. He died on August 20, seven days after admission. The clinical diagnosis was that of leaking intracranial aneurysm.

Summary of Necropsy. (*P.M.* 361, 1930.)

Metastatic glioma of leptomeninges of spinal cord and cauda equina. Primary glioma of left frontal lobe and corpus callosum. Moderate hypertrophy of left ventricle of heart. Moderate atheroma of mitral valve, of commissure, descending thoracic and abdominal parts of aorta, and of coronary and common iliac arteries. Ante-mortem thrombus (11 by 1·5 cm.) in heart. Similar thrombus (17 cm. long) in left common and external iliac veins. Congestion of lungs. Thymus replaced by fat. Colloidal adenoma (1·5 cm. in diameter) in lower pole of right lobe of thyroid. Moderate congestion and parenchymatous degeneration of liver and kidneys. Slight œdema of spleen. Fatty

infiltration of pancreas. Mucous catarrh and congestion of stomach. Obliteration by fibrosis of terminal part of vermiform appendix. Marginal and internal hæmorrhoids. Petechial hæmorrhages in mucosa of urinary bladder. Black gravel in prostate. Congestion of fatty marrow of upper half of shaft of left femur. Papilloma of skin above inner canthus of right eye. Valvular patent foramen ovale (*ca.* 0·5 cm. in diameter). Well nourished, well developed man, showing frontal and vertical alopecia.

Macroscopic Examination.

Brain.—There was venous engorgement of the surface of the cerebral hemispheres. A tumour (5·5 by 4 by 4·7 cm. from before backwards) occupied the head of the left caudate nucleus, the adjacent part of the genu and anterior third of the body of the corpus callosum, and the adjacent white matter of the left frontal lobe. It consisted for the most part of soft greyish-white granular tissue, but was in places opaque yellow. The frontal horn of the left ventricle was situated immediately behind and below the tumour, and was compressed so as to form a crescentic slit. In this region its ependymal lining, in an area 1·5 cm. diameter, presented several glistening granulations. The body of the left lateral ventricle was obliterated by downward projection of the tumour in the body of the corpus callosum. This part of the tumour had displaced the septum lucidum and fornix to the right, and was adherent to the fornix in places. The posterior horn of the right lateral ventricle was slightly dilated but there was no other evidence of hydrocephalus. The third and fourth ventricles appeared normal.

On the ventral aspect of the left lateral lobe of the cerebellum the leptomeninges were opaque and slightly raised over small ill-defined confluent areas which together measured 1·8 by 1·2 cm. On the dorsal aspect the leptomeninges over the vermis contained a few ill-defined greyish-yellow nodules (up to 0·2 cm. in diameter).

Spinal cord.—The leptomeninges of the spinal cord were extensively infiltrated by opaque gelatinous grey growth. This growth formed rounded nodules on the posterior roots at various levels, and in places it formed a coat of confluent nodules over the posterior surface of the cord and adjacent nerve roots. The cervical part of the cord showed very little deposit, but there were a few small nodules (up to 0·5 cm. in diameter) over the origins and along the course of some posterior roots, especially on the second cervical root on the left side. From the eighth cervical to ninth thoracic segments the cord was covered by a continuous sheet of tumour tissue, and below that its surface was studded by grey bosses of growth (up to 1·0 by 0·7 cm.). On the cauda equina the deposit was not quite so heavy; numerous nodules of soft grey growth (up to 1·0 by 0·5 cm.) were attached to the roots, and there was also a diffuse deposit in the arachnoidea, which was most conspicuous at the points of exit of the posterior nerve-roots through the dura. The anterior surface of the cord showed a few diffuse areas of infiltration (up to 1·2 by 0·3 cm.), mostly situated in the middle line over the linea splendens in the lumbar region.

Microscopic Examination.

The primary tumour.—The greater part of the centre of the tumour in the left frontal lobe and genu of the corpus callosum is necrotic. Outside this the tumour, in the frontal lobe, is of loose texture and is composed of cells with round, oval or spindle-shaped nuclei, the majority of which have thin membranes, a fine chromatin net beset with a few nodes of variable size, and one or two nucleoli. Some of the nuclei, however, contain much more chromatin. The cells are stellate or spindle and their cytoplasmic processes frequently contain neuroglial fibrils when stained by Mallory's method. There is a moderate number of multinucleate giant cells but mitotic figures are not present. In some cells there are one or two dots in the cytoplasm, near the nucleus, which resemble blepharoplasten but are probably diplosomes because in the giant cells there are sometimes as many as five or six. Palisades of spindle cells are sometimes present at the border of an area of necrosis, but there is no special arrangement of the cells in relation to vessels. In the corpus callosum the cells are closely packed; they are of spindle form and contain conspicuous neuroglial fibrils (fig. 12). These cells are impregnated by Cajal's method. In the more spongy parts of the tumour there are many typical fibrillary astrocytes.

The margin of the necrotic tissue is in places honeycombed with a number of small, greatly engorged, thin-walled vessels, in some of which there is endothelial proliferation. In this region also there is considerable fatty degeneration. Where the tumour projects into the left ventricle the ependyma has been replaced by growth. There are miliary implantations of tumour tissue in the ependyma adjacent to the primary mass.

Cerebellar metastases.—The leptomeninges over the cerebellum are in places infiltrated with finely fibrillated glial cells of stellate and spindle form, similar to those observed in the primary tumour. These cells tend to be arranged with their long axes at right angles to blood-vessels and to the surface of the arachnoid membrane. There is a conspicuous endothelial proliferation in the small blood-vessels that lie in this tissue. The amount of reticulum is scanty. The tumour cells do not invade the cerebellum nor penetrate into the sulci.

A small nodule in the leptomeninges over the vermis proves to be a minute psammomatous endothelioma arising in the arachnoid.

The spinal metastases.—In the second thoracic segment the subarachnoid space is occupied by gliomatous tissue similar to that seen in the leptomeninges of the cerebellum. The tissue is relatively thin over the ventral surface of the cord but increases over the lateral aspects, and over the posterior columns it reaches a maximum depth equivalent to a quarter of the total depth of the posterior columns. There is no invasion of the cord. In the twelfth thoracic segment a boss of similar tissue is seen surrounding the right dorsal root (fig. 13). The tissue is loose in texture and contains many stellate cells and bands of spindle cells that are arranged at right angles to the arachnoid membrane. Amongst these are occasional multinucleate forms. The tissue is moderately vascular and there is a conspicuous degree of endothelial proliferation in the vessel walls.

In the cauda equina the deposits present a similar appearance. In these there is no evidence of fatty degeneration. The cells are not impregnated by Cajal's method, but with Hortega's silver carbonate method for astrocytes a great number of fibrillary astrocytes is seen (fig. 14). Many of these have foot-plates in relation to strands of collagen and adjacent nerve bundles. Amongst the astrocytes are many spindle bipolar forms.

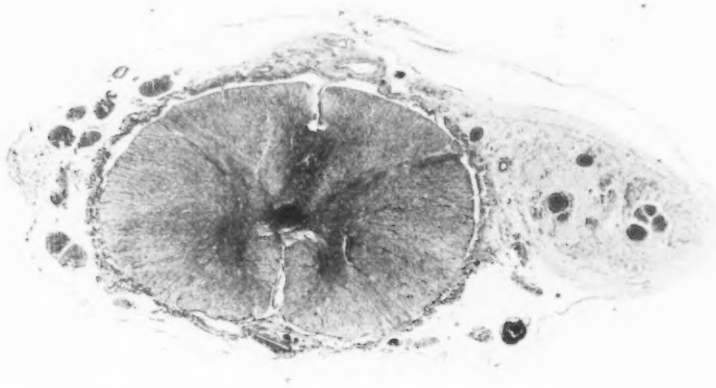

FIG. 13 (*Case* 6).—Transverse section of twelfth thoracic segment. Metastatic mass of growth in subarachnoid space on the right. Phosphotungstic acid hæmatoxylin. × 8.

Comment.—In judging the nature of this glioma the form of the tumour cells in the spinal deposits is important. In these deposits many of the astrocytes are attached by foot-plates to the collagen strands and nerve fibres. This proves that they are cells which have grown *in situ* and have not merely been carried to their present position. From the macroscopic and microscopic appearances it is impossible to regard the deposits as developmental rests, and developmental rests have never been recorded over the cauda equina as far as we are aware. There can be no doubt that the deposits are metastases.

In the primary tumour the polymorphism of cell forms, the presence of giant cells and the extensive necrosis are in accordance with the descriptions given by Bailey and others of glioblastoma multiforme. The tumour has, therefore, been provisionally labelled as an example of this type. The very large proportion of astrocytes, both in the primary tumour and in the metastases, raises the question as to whether the tumour should not be regarded as an astrocytoma that has undergone anaplasia with the development of more embryonic glial forms and a higher order of malignancy. Such a change occurring in an astrocytoma

has already been reported by Bailey and Cushing [4]. The predominance of elongated spindle forms in the corpus callosum (fig. 12) is perhaps the result of pressure upon the tumour in this site forcing the cells into a minimal space. A parallel observation is afforded by Case 7 in which a large proportion of spindle cells was present in an astrocytoma situated in the left optic thalamus. The variations in morphology of gliomas that may be produced by the varying texture of different parts of the brain is a subject worthy of closer study.

In the metastases the tumour cells occupy the subarachnoid space. Here they have room to grow, and it is probable that they show more clearly their true form than when multiplying in the substance of the brain. Their astrocytic character is very conspicuous (fig. 14). Had the growth in the brain alone been available it might have been argued that the astrocytes were formed by a reaction of normal tissue when invaded by tumour cells. The structure of the spinal metastases effectively rules out this objection.

Astrocytoma.

Case 7.—This case has been previously reported by us [16], and it is only necessary, therefore, to mention the main facts here. The case was one of astrocytoma in the right optic thalamus in a man aged 28. The tumour invaded the lumen of the third ventricle and extended up to the leptomeninges between the corpus callosum and pineal gland. The inner surface of the spinal arachnoidea was studded with numerous glistening grey nodules, up to 0·1 cm. in diameter, which on section proved to possess the same structure as the primary tumour. Doubt has been cast upon our interpretation of these nodules by Bailey and Bucy [3], who consider that "it is a little difficult to believe that an astrocytoma could produce such an infiltration or metastasis." They prefer to believe that the nodules we described were islands of neuroglia analogous to those found in the spinal arachnoidea by Wolbach [21] and others in cases in which there was no primary glioma of the brain, and thus no question of metastases in the spinal cord or its membranes. This interpretation of our case is incorrect, for, as the original case report stated, numerous nodules of tissue identical with those in the spinal arachnoidea were found in the arachnoidea over the pineal body, near the primary tumour. These nodules were identical in structure with the parent tumour, and they were only found in the cerebral subarachnoid space in the vicinity of the primary tumour. Moreover, in the cases alluded to by Bailey and Bucy the neuroglial nests were associated

with other gross developmental abnormalities of the central nervous system, such as tuberose sclerosis and, as far as we are aware, they have not been found in an otherwise normal central nervous system.

Ependymal Glioma.

Case 8.—Ependymal glioma of cerebellar vermis extending through the foramen magnum. Progressive quadriplegia. Death.

History: Alfred D., aged 59, a retired police officer, was admitted to the Hospital for Epilepsy and Paralysis, Maida Vale, under the care of Dr. Russell Brain, on November 8, 1929. He had contracted syphilis at the age of 26, but apart from this had been quite well until May, 1926, when he began to have numbness in the tips of the fingers and weakness of the right hand. The numbness gradually extended up to the right elbow, and two or three months later the right side of the neck was similarly affected. In May, 1927, he began to drag his left foot occasionally. He noticed that his "stomach muscles" seemed stiff and he complained of a lifeless kind of feeling. There does not appear to have been much further change until July, 1929, when his walking became difficult owing to loss of power, and micturition became frequent. His left upper limb was also affected at this time.

Examination: The following neurological signs were found: Slight relative analgesia on the left side of the face. Weakness and wasting of all the muscles of both upper limbs and shoulder-girdles, more marked on the left side. Weakness of the abdominal muscles. Weakness and slight spasticity of both lower limbs. Exaggeration of all tendon-jerks except the right ankle-jerk, which was absent. Absence of abdominal reflexes. Bilateral ankle clonus and extensor plantar reflexes. Sensibility to light touch was preserved. There was patchy analgesia to pin-prick over the radial borders of both upper limbs, and in the lower limbs. Sensibility to heat and cold was lost up to the fifth cervical segmental level on both sides. Postural sense was lost in the digits and appreciation of vibration was diminished in both lower limbs, especially on the left side. The Wassermann reaction in the blood was negative.

Lumbar puncture yielded fluid clear and colourless. Total protein, 0·04 per cent. approximately; 1 to 2 cells per cubic millimetre. Wassermann reaction negative.

A diagnosis of syringomyelia was made. By November 24 he was definitely weaker and there was occasional incontinence of urine. On December 23, increasing helplessness was recorded. There appeared to be definite reduction in discrimination between sharp and blunt, especially in the lower limbs. At times there was cutaneous tenderness in the left lower limb and left side of the trunk. On January 14, 1930, his general condition was much worse. There was marked respiratory distress, cyanosis and laryngeal rattle. He died on this day.

Macroscopic Examination.

Post-mortem examination was limited to the brain and spinal cord.

Brain.—A solid, firm tongue-shaped tumour (5 cm. long by 3·5 cm. wide by 2 cm. deep) projected from beneath the lower extremity of the vermis to fill the cisterna magna and extend over the posterior surface of the medulla oblongata and first segment of the cervical cord. The surface of the upper part of the tumour was broken up into cauliflower-like nodules, but the lower portion had a smooth greyish-yellow glistening surface marked by a few fine blood-vessels. On median sagittal section the tumour appeared as a triangular mass, the base of which rested against the posterior surface of the flattened medulla and upper cervical cord. It extended into the lower part of the fourth ventricle, reaching as high as the lower borders of the choroid plexuses to which it was adherent. The margins of the growth were everywhere sharply defined. The cut surface was flat, firm and glistening greyish-white and was broken up into lobules (up to 0·2 cm. diameter) by a fine grey network. It was gritty to the knife in many places, especially near its posterior surface. The remainder of the brain appeared normal.

Spinal cord.—Beneath the arachnoid membrane on the posterior surface of the fifth thoracic segment there was an inconspicuous group of glistening pin-head nodules which were only observed on close examination after fixation. In the light of previous experience these were suspected of being fragments of metastatic tissue.

Microscopic Examination.

The median cut surface of the tumour was examined in three blocks and transverse sections were taken from the lower part of the medulla oblongata and from the fifth thoracic segment of the cord.

The primary tumour.—The tumour is composed of a solid mass of cells which vary somewhat in appearance and arrangement in different places. By far the greatest part is made up of long spindle-shaped cells (fig. 15), which tend to lie in interlacing bundles and often arrange themselves at right angles to blood-vessels and strands of collagen. Their cytoplasm is full of stout neuroglial fibrils (phosphotungstic acid hæmatoxylin). There is a variable number of such fibrils in each cell; in some there are as many as twelve. These fibrils are readily demonstrated with silver, but are only faintly stained by Cajal's gold chloride sublimate. In addition, there are in the majority of the cells conspicuous blepharoplasten situated in the cytoplasm close to the nucleus. The nuclei are round or oval and have a delicate membrane and chromatin net beset with a moderate number of nodes. From one to three nucleoli are present in the majority of cells. There is no evidence of foot-plates in connection with these cells in either Cajal or silver preparations. In other parts of the tumour there are small, poorly-defined areas composed of irregular groups of polygonal cells with round nuclei (fig. 16). These cells have no processes and no neuroglial fibrils. Occasionally they appear to be grouped about a small lumen. In such places the blepharoplasten are collected in the cytoplasm adjacent to this lumen, but cilia are not demonstrable. There is

considerable "calcification" of the tumour, especially at the periphery and adjacent to the posterior border. The blood-vessels, which are not numerous, frequently show a proliferation of endothelial cells, and many have undergone a hyaline collagenous thickening. The blood-vessels and a scanty stroma of collagen and reticulum divide the tumour into poorly-defined lobules. Apart from this stroma there is no reticulum in the tumour.

The tumour tissue involves the ependyma of the roof of the fourth ventricle, but does not invade the choroid plexuses, which appear normal. The posterior border of the tumour extends into the leptomeninges as small polypoid projections. The tissue forming these projections and the adjacent tumour is extremely rich in neuroglial fibrils.

The spinal metastases.—In the section of the fifth thoracic segment there are two small oval nodules of solid tumour tissue situated immediately beneath but not attached to the arachnoid membrane over the posterior aspect of the cord. These nodules are chiefly composed of interwoven neuroglial fibrils, amongst which are a few nuclei similar to those of the primary tumour. Each nucleus is surrounded by a little ill-defined cytoplasm. In one of the cells a group of three blepharoplasten lying in a clear halo is seen near the nucleus. Neither collagen fibres nor vessels are seen in these nodules.

Comment.—This tumour is an ependymal glioma and is particularly interesting because its cells contain conspicuous fibrillæ (fig 15). It is generally supposed that the presence of such fibrillæ in neuroglia indicates that the cells are astrocytes, but our experience has shown that ependymal spongioblasts are more commonly and more conspicuously fibrillated than has hitherto been recognized. In this tumour, for example, the cells are clearly not astrocytic in nature, for they do not form foot-plates and they are not impregnated by Cajal's method. Further, they contain conspicuous blepharoplasten, and in some parts of the tumour tend to arrange themselves in the rosettes of Bailey. The site and macroscopic appearances are fully in accord with the histological diagnosis of ependymoma.

The nodules in the subarachnoid space of the spinal cord presented meagre material for microscopic diagnosis. They bore a considerable resemblance, however, to the parent tumour, and the finding of blepharoplasten established their origin. The fact that metastasis could occur in so relatively benign a tumour lends strong support to our view that the potentiality of a glioma to disseminate metastases in the cerebrospinal pathway depends as much upon the site of the tumour in relation to this pathway as upon the intrinsic malignancy of its component cells.

Although ependymal gliomas are of slow growth and relatively benign, it is not unlikely that they frequently give rise to spinal metastases, for when they arise in relation to the fourth ventricle, a

common site, they tend to project into the cisterna magna and even into the subarachnoid space of the cord, from which position spinal metastases can easily occur. Spiller [18] recorded a case of ependymoma of the posterior part of the fourth ventricle which spread down on the cord to the sixth cervical segment; another but smaller tumour of similar structure was found on the lower thoracic region of the cord "and was probably a metastatic growth." Bailey [1] stated that he had examined sections of this tumour and was convinced that it arose from ependymal cells in the floor of the fourth ventricle.

Discussion.

Our search for spinal metastases began only in 1928, and since then we have found them in eight out of twenty-two cases of cerebral glioma in which both brain and cord were examined. In addition, we have found during the same period one case of sarcomatosis (or possibly gliomatosis) of the leptomeninges of both brain and cord without a demonstrable primary tumour, one case of bilateral acoustic nerve tumours, in which there were numerous unsuspected spinal ependymomas and tumours of the meninges and spinal nerve roots, and one case of pituitary adenoma with dissemination of free tumour cells in the spinal subarachnoid space. From our cases it appears that spinal or cerebral metastases may be found in the following varieties of glioma: medulloblastoma, neuro-epithelioma of the retina, glioblastoma multiforme, astrocytoma and ependymoma.

Other varieties can be added from cases reported in the literature. Thus, van Wagenen [20] has made it clear that *papillomas of the choroid plexus* may also be disseminated in the way we have described. In one of his cases the primary tumour filled the greater part of the left lateral and third ventricles. There were "many small implants" in the left temporal horn and a solitary nodule of similar tumour tissue in the occipital pole of the right lateral ventricle. The macroscopic and microscopic appearances of this type of tumour are so characteristic that van Wagenen is able to cite from the literature other cases in which a primary papilloma of one or other choroid plexus gave rise to similar ventricular or subarachnoid implants. In one of these, reported by Töppich [19], a papilloma occupying the fourth ventricle was associated with numerous secondary deposits in the cerebral and cerebellar leptomeninges and, in addition, the subarachnoid space from the middle thoracic region to the cauda equina contained very numerous, often confluent masses of tumour. Davis and Cushing [8] believe that

the choroid plexus tumours are usually single and that they may be confused with papillary ependymoma, a tumour that "tends to seed itself." We have, however, in this Institute an undoubted papilloma of the fourth ventricle (P.M. 224, 1923), and in this specimen the roof of the fourth ventricle is studded with minute nodules of growth. The spinal cord was not examined. There can be no question but that this type of tumour is liable to give rise to metastases.

Oligodendroglioma may also in certain circumstances give rise to metastases. Thus in a case previously reported [6] from Dr. Cushing's clinic, a man aged 23 died suddenly three and a half years after removal of an oligodendroglioma of the right frontal lobe, and at necropsy was found to have secondary tumours in the occipital horns of both lateral ventricles and in the fourth ventricle.[1] [2]

Earlier literature contains many reports of cases in which gliomas gave rise to metastases, but most of the histological descriptions are inadequate for the purposes of modern classification.

The extent of metastasis varies greatly in different varieties of glioma and is approximately proportional to the malignancy of the primary tumour, estimated by clinical and histological criteria. Thus in medulloblastoma and neuro-epithelioma of the retina the metastases are profuse. These tumours, indeed, appear to spread as much by direct extension as by metastasis. Thus in Case 3 (medulloblastoma) tumour tissue was found as a continuous sheet over the whole surface of the third and lateral ventricles, and there were isolated nodules of tumour in the spinal subarachnoid space. In Case 2 (neuro-epithelioma of the retina) there was a continuous sheet of tumour tissue throughout the basal cisterns and subarachnoid space of the cord, while isolated nodules of tumour were found on the convex surface of the brain and in the ventricles. The metastases of these tumours alone (Cases 2, 3 and 4) infiltrate the nerve tissue of brain and cord from their position in the meninges, though in other less malignant types the metastases infiltrate the meninges, the walls of the ventricles and, in Case 5, the sheaths of spinal nerve roots.

In glioblastoma multiforme (Case 6), and in another tumour of primitive type as yet unclassified (Case 1), the metastases were large and

[1] This case has also been reported by Bailey and Bucy [2] in their study of oligodendrogliomas.

[2] Recently Purdon Martin (*Brain*, 1931, **54**, 334) has reported another case of oligodendroglioma that spread, partly in continuity and partly by metastasis, through the greater part of the ventricular system.

surrounded the cord. In Case 5, a medulloblastoma of less malignant type than in Cases 3 and 4, there were large isolated nodules of tumour in the third and lateral ventricles, and there were smaller isolated flecks of metastatic tissue in the spinal subarachnoid space. In the two other cases (Case 7, astrocytoma, and Case 8, ependymoma) the metastases were scarcely visible to the naked eye and appeared under the microscope as small nodules lightly attached to the arachnoid and evidently possessing no powers of invasion. Criticism has been levelled by Bailey and Bucy against our diagnosis of the spinal nodules as metastases in Case 7. This is answered in the comment on the case as reported in this paper. The spinal nodules found in the case of ependymoma (Case 8) consisted for the most part of neuroglial fibrils, but blepharoplasten were found, thereby establishing their relationship to the primary tumour.

The Spread of Gliomas.

Gliomas may spread in continuity or by metastasis. We are not directly concerned in this paper with spread in continuity, but it is necessary to mention briefly some of the features of that process, inasmuch as the tumours that we are considering often spread in the subarachnoid space in this way. When enclosed by nerve tissues most gliomas appear to spread centrifugally by direct extension independently of vascular channels. But when a tumour, especially one of the more malignant varieties of glioma, reaches the leptomeninges, it may again invade the brain from the surface, not only by direct extension but also by spreading along the perivascular spaces. In this position also a glioma may extend through the leptomeninges and in rare instances may even invade the adjacent dura and bone. We have studied one example of glioblastoma multiforme situated in the temporal lobe which invaded the tegmen tympani.

Metastases from gliomas appear to be limited to the central nervous system and to be disseminated by the cerebrospinal fluid. They occur in the walls of the ventricles or in the pia arachnoid of the brain and cord. In the ventricles the metastases vary in size from nodules that are easily seen with the naked eye to microscopic collections of cells. The ependyma is raised up at the margins of the nodules, but is usually deficient over their summits. The metastases undoubtedly reach this site by way of the ventricular cavities; they do not appear to be related to the subependymal vessels. All the evidence suggests that implants from the primary tumour may gain entrance to the subependymal glia by splits or cracks in the ependyma such as are frequently seen in

severe hydrocephalus. It is also conceivable that they may be deposited upon and replace the intact ependyma, but histological evidence of such a process has not been seen. Internal hydrocephalus was demonstrated at some period in all of our cases in which ventricular spread occurred.

Spinal metastases appear to arise by implantation along the subarachnoid space, for they are limited to, or at least are most numerous in, that situation. They are also more frequently seen on the dorsal than on the ventral surface of the cord, from which it may be surmised that gravity plays a considerable part in their distribution. Gravity may also account for the situation in the occipital and temporal horns of the ventricular metastases found both in Case 5 and in the example of oligodendroglioma of the right frontal lobe cited above.

A perusal of our cases shows that, with the exception of Case 2, all the primary tumours had reached the surface of the ventricular system although they varied considerably in malignancy. Case 2 was a glioma of the retina which spread rapidly along the optic nerve to reach the cisterna chiasmaticus. There can be no doubt that access to the ventricular system or basal cisterns is a circumstance of primary importance in the production of metastases. The intrinsic malignancy of the tumour plays its part in promoting rapid growth to the ventricular or subarachnoid surface of the brain and thereafter in the formation of potential metastatic tissue, but a relatively benign tumour that arises in or near these surfaces will also be liable to seed itself in proportion to its accessibility and the exuberance of its growth. The only spread of relatively benign primary tumours of other parts of the body that is at all comparable to this appears to be that of papilloma of the bladder, or that of pseudomucinous cystadenoma of the ovary in the peritoneal cavity.

Histological Features of Metastases

There is a certain amount of evidence suggesting that gliomas vary in their morphology to some extent in accordance with the texture of the nervous tissue in which they grow. Thus, glial tumour cells invading the white matter of the brain tend to adopt a spindle form and to lie in parallel bundles between the myelin sheaths. They also tend to assume a spindle form in areas where the brain is at all extensively replaced by connective tissue. Allowances have to be made for such circumstances in determining the nature of the type cell in gliomas. Considerable light may be shed on this problem in individual cases by a study of the cytological features of the metastases, because it is then possible to see

the tumour cells growing on a free surface and untrammelled by their supporting tissue. In the more malignant tumours (Cases 2, 3, 4, 5) the metastases closely resembled the parent tumour. In Case 1 study of the cells in the leptomeninges was of great assistance in determining the morphology of the tumour cells, inasmuch as they were better preserved and the character of their processes was more easily seen (fig. 2).

In Case 6, glioblastoma multiforme, the metastases were of the greatest value. The primary tumour in the corpus callosum was composed of fibrillated cells, the majority of which were of spindle form (fig. 12) while others were astrocytes. It was difficult to determine how many of the astrocytes observed were true tumour cells and how many were the result of glial reaction in the invaded brain tissue. The structure of the metastases, however, clearly showed that the majority of the tumour cells were adult fibrillary astrocytes (fig. 14). Many of these had developed *in situ* because their foot-plates were attached to the collagen sheaths of the nerve roots and other fixed structures in their environment.

In the less rapidly-growing kinds of tumour, the presence of gliomatous metastases in the leptomeninges leads to a focal proliferation of the connective tissue with increase of reticulum fibres. In some places these fibres ramify between the individual tumour cells, but in others cellular areas devoid of reticulum are found. The appearances produced by this proliferative reaction of connective tissue resemble at times those seen in so-called "primary sarcomatosis" of the meninges. In this condition there is a profuse production of reticulum and the tumour cells tend to invade the underlying brain by the perivascular sheaths alone. These features have been regarded as characteristic of sarcomatosis, but our cases of gliomatosis show that they are not so.

Associated with gliomatosis there is often a proliferation of the meningeal capillaries furnishing the neoplastic tissue with an increased blood-supply. This was conspicuous in Case 6. The capillaries in this example often showed also an endothelial proliferation as in the primary tumour.

Metastatic deposits often undergo focal degeneration and necrosis. This is accompanied by an infiltration in and about such areas with neutrophil leucocytes. More rarely (Case 1) plasma cells are also present.

No reaction on the part of the ependyma or of the subependymal glia has been observed in connection with ventricular metastases.

Clinical Significance.

Lumbar puncture was done at some stage of the illness in five of the eight cases described above and the total protein content was found to be raised in three cases, particularly in Cases 1 (unclassified glioma) and 6 (glioblastoma multiforme), where it reached 0·5 per cent. In both of these cases there were extensive spinal metastases, but in Case 6 the primary glioblastoma multiforme of the corpus callosum had spread to the surface of the left lateral ventricle, and the rise of protein in the cerebro-spinal fluid may have been in part due to bleeding from the primary tumour into the ventricle. We have observed a case of vascular glioblastoma multiforme of the corpus callosum in which the protein content of the spinal fluid was 0·15 per cent., though no spinal metastases were found at necropsy. A similar rise of protein in the cerebro-spinal fluid obtained by lumbar puncture has been observed by us in association with tumours of the cerebello-pontine angle, in one case of dural endothelioma of the sphenoidal ridge (0·25 per cent.), and in a glioma (spongioblastoma unipolare) invading the left lateral ventricle. It is thus clear that increase of protein in the spinal fluid in cases of intracranial tumour does not necessarily indicate the presence of spinal metastases. However, it should probably be regarded as suggestive of that complication when it is encountered in children, for the other causes of such an increase occur almost exclusively in adults. Our cases also show clearly that increase of protein in the spinal fluid, in the presence of signs and symptoms suggesting spinal metastases, does not indicate that the primary tumour is always a medulloblastoma of the cerebellum.

Tumour cells were not recognized in the spinal fluid in any of our cases, though recent observation of tumour cells in the spinal fluid from a case of rapidly-growing pituitary adenoma suggests that they might be found more often if looked for carefully. The presence in the spinal fluid of mononuclear cells other than lymphocytes should always arouse suspicion of tumour.

The metastasis in the third ventricle in Case 8 probably accounted for the polyuria observed before operation, but apart from that no symptoms were observed in our cases that could be definitely attributed to the cerebral metastases. Bielschowsky and Unger [5] reported a case in which a tumour was removed from the left motor area, and subsequent necropsy showed that the tumour removed at operation was a metastasis from a primary papilloma of the choroid plexus of the fourth ventricle.

It is remarkable that in our cases spinal metastases gave rise to few

or no signs, even when the cord was almost entirely surrounded by large masses of tumour. Cushing [7] has reported several cases in which signs of compression were produced by spinal metastases of cerebellar medulloblastoma after removal of the primary tumour. In one of his cases Elsberg [9] removed a metastatic tumour from the cauda equina fourteen months after Cushing had removed the primary tumour. The patient died six months later from recurrence in the cerebellum.[1] So far as we are aware clinical symptoms from spinal metastases have hitherto been observed only in the malignant varieties of glioma, but with the increasing success of attempts to remove completely the more benign gliomas it is possible that spinal metastases from these tumours may have time to grow to such a size as to produce symptoms. There are, of course, other diffuse tumours of the leptomeninges that may give rise to spinal symptoms, for example, primary sarcomatosis, or secondary carcinomatosis of the leptomeninges. Some writers (Ford and Firor [12]) have sought to describe distinctive symptom complexes for primary sarcomatosis of the leptomeninges, but it is clear from their own work that the clinical features only serve to indicate the presence of diffuse tumours of the leptomeninges and do not necessarily indicate the pathological type of tumour.

The proposition has to be considered that metastasis may be promoted in certain cases by operative interference. This probability arises chiefly in conjunction with tumours in the neighbourhood of the fourth ventricle. Thus, in a case recorded in this Institute a patient died a few hours after removal from the posterior fossa of a meningeal tumour which had become somewhat adherent to the adjacent cerebellum. There was considerable gliosis of the cerebellar margin. On examination of the spinal cord, four minute pin-point and pin-head nodules were observed under the arachnoid membrane over the dorsal surface of the sixth thoracic segment. On microscopic examination these proved to be free-lying nodules of neuroglia identical in appearance with the cerebellar tissue that had been adherent to the meningeal tumour. After removal of gliomas that are in contact with the basal cisterns, especially the cisterna magna or the walls of the ventricles, the question of prophylactic irradiation of the spinal canal and ventricular regions should receive consideration.

[1] Collier (*Brain*, 1904, **27**, 506) reported a case in which spinal metastases arose from a tumour in the neighbourhood of the fourth ventricle. Severe shooting pains occurred in all the limbs and later the knee, wrist and elbow jerks were lost, and the fifth and sixth cervical nerves were completely paralysed.

Study of cases such as we have described in this paper will help considerably in enabling clinicians to distinguish between the cases that can be benefited by surgical treatment and those that are hopeless. Operation is not necessarily contra-indicated when metastases are found, for it still remains to be seen whether the small metastases observed in the more benign gliomas will grow so as to produce symptoms. But in the presence of extensive metastases malignant gliomas, like those described in Case 4, are clearly not suitable tumours for operative treatment. To consolidate the great advances recently made in neuro-surgery, it is necessary that we should learn to recognize such cases without recourse to operation.

SUMMARY.

Eight cases are reported in which a primary glioma of the brain was associated with subarachnoid spinal metastases and, with the exception of Cases 7 and 8, with intracranial metastases as well. These cases include the less malignant and more highly differentiated types of glioma, such as astrocytoma and ependymoma, as well as the more primitive and malignant types, such as neuro-epithelioma of the retina, medulloblastoma and glioblastoma multiforme.

It is shown that the proximity of a glioma either to the ventricular system or to the basal cisterns is probably as important in promoting metastases as the intrinsic malignancy of the tumour cells.

The secondary deposits in the subarachnoid space have room to grow freely, and a study of their cytology sometimes throws considerable light on the nature of the primary growth.

Attention is drawn to the alterations in the cerebrospinal fluid and other clinical disturbances that may arise in these cases.

Inasmuch as spinal metastases have been observed in eight out of twenty-two consecutive full necropsies in cases of glioma, it is evident that the frequency of this process has hitherto been underestimated.

We desire to thank Professor H. M. Turnbull for his help in the preparation of this paper and our colleagues for permission to use the clinical records of their cases.

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A CASE OF CONGENITAL ELEVATION OF THE SCAPULA (SPRENGEL'S DEFORMITY) WITH DEFECT OF THE CERVICAL SPINE ASSOCIATED WITH SYRINGOMYELIA.

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CASES of Sprengel's deformity of the shoulder, a comparatively rare condition, have been reported associated with a great variety of developmental abnormalities. As far as could be ascertained, however, only one case has been recorded in which the deformity was associated with sensory disturbance and paraplegia [1].

A male, aged 34, an electrician, was admitted under Dr. Gordon Holmes, to the National Hospital, Queen Square. He complained of numbness and weakness of the hands, and numbness, weakness and stiffness of the legs. The disability commenced about two years previously. He stated he was born with wry-neck and wore an iron frame up to the age of 12. His health had been good until the onset of the present condition.

Just over two years prior to admission he injured the three middle fingers of his left hand in the door of a railway carriage. They were contused and lacerated, but he continued his work and the wound healed normally. About four months later he became aware of a numb feeling in the tips of all the fingers of this hand, and clumsiness in using them, especially in manipulating small objects, as small screws and fine tools. Soon afterwards he developed a dull aching pain, not severe, extending from about the junction of the middle and lower thirds of the left thigh down to about the middle of the left calf. It was more or less constant but definitely aggravated by exercise and eased by rest. It lasted several months, gradually diminishing in severity and finally disappearing. The onset of the pain was quickly followed by the development of numbness in the area of its distribution. On touching that part it felt "numb and dead." The numbness gradually became more intense and spread upwards and downwards. At the same time he noticed a gradually progressive loss of power of this leg. The limb felt heavy and clumsy and swung outwards when he walked. He became unstable on his feet and tripped easily.

Up to six months prior to admission the condition had advanced very slowly, but from then onwards progress had been much more rapid. At that time the fingers of the right hand and the toes of the right foot had also become numb. On admission his left arm, the left half of his chest, right hand and

forearm, his left leg below the middle of the thigh, and the whole of the right leg "felt numb," and his arms and legs felt weak.

There have never been sphincter, visual or auditory disturbances, and he has never had convulsions, headaches, or vertigo.

He comes from a healthy family with no history of a similar condition.

Physical examination.—He is muscular and healthy-looking. His head is inclined to the right and there is marked asymmetry of the head, face and chest as seen in the photographs (fig. 1). The neck is very thick and remarkably short, the distance from the occiput to the seventh cervical vertebral spine being only about 2 in. The muscles of the neck stand out prominently on the

FIG. 1.—Photographs showing the deformity of the left shoulder, the shortness of the neck, the scoliosis, the tilting of the head, the asymmetry of the face and the over-development of the mammæ. The border of the scapula and the position of the vertebral spines have been marked out in ink.

left, especially the upper part of the trapezius, which is firm on palpation. All the movements of the head and neck are extremely limited. The right scapula is normal in position but the left is considerably higher, and a bony projection from the inner part of its superior border can be felt under the trapezius and seen in the skiagrams. A bridge of bone, also visible in skiagrams, extends from the transverse processes of the sixth and seventh cervical vertebræ to the upper part of the vertebral border of the scapula, where it articulates with this bone. The scapula is almost fixed and permits of very little movement. Its vertebral border stands out prominently, separated from

the thorax. Movement of the left arm at the shoulder is normal in all directions up to the horizontal, but above this, because of the degree of immobility of the scapula, it is very limited. The right upper arm is $\frac{3}{4}$ in. less in circumference than the left, but of the same length. The forearms and hands are symmetrical and equal in size. The left leg is uniformly thinner than the right, being 1 in. less in circumference. There is no difference in length. He states that this has been so with the arm and leg since childhood.

The mammæ, especially the left, are over-developed and he has a noticeably protuberant belly. The skin over the trunk is moist and greasy, showing obvious vasomotor and pilomotor disturbance. On the ball of the right thumb there are scars of burns by cigarettes, although he had never been aware of pain and discomfort.

Speech and articulation are not disturbed and his mental functions are normal.

The retinæ and optic discs are normal. The pupils are moderate in size, but the right one is slightly larger than the left. Neither is quite circular but both are central and regular. The direct and consensual reactions to light are somewhat sluggish, especially those of the right. Both react normally on convergence. There is well sustained and regular horizontal nystagmus in both eyes on deviation to the right and left, but slightly faster on looking to the left. The left palpebral fissure is narrower than the right; this is part of the general facial asymmetry. There is no ex- or en-ophthalmos.

Motor system.—He is right-handed. The right biceps, although normal in consistence and action, is definitely smaller than the left. On the left the rhomboids, latissimus dorsi and serratus magnus are smaller than normal.

Power of certain movements is defective on both sides. Abduction of both shoulders, external rotation on the right, and external and internal rotation on the left, are weak. On the right supination and pronation, and on the left supination, are weak. The right and left long extensors of the fingers are feeble. There are no involuntary movements. Slight inco-ordination, with an error of projection, is present on the left but not on the right, in "finger—nose—finger" tests. Posture is maintanied normally. There is a noticeable increase of flexor tone, clasp-knife in type and greater on the right. Finer and alternate movements are poorly performed, especially on the right.

The intercostal, spinal and abdominal muscles are normal. There is no localized bulging of the abdominal wall on coughing, or deviation of the umbilicus on attempting to sit up.

Although the left leg is thinner than the right, there is no definite wasting of the muscles. Power is not appreciably impaired in either leg. There is marked bilateral spasticity of the clasp-knife variety. Incoördination is noticeable on both sides, but is greater on the right. Posture is normal.

Reflexes.—All the tendon-jerks are symmetrically much exaggerated. A jaw-jerk is present and there are well-marked finger-jerks on both sides. The legs are thrown into clonus even on comparatively gentle manipulation. There is well-sustained ankle-clonus on both sides. Both plantars are extensor. The upper abdominal reflexes are much reduced and the lower ones are absent.

Sensory system.—There is much disturbance and dissociation of cutaneous sensibility. Appreciation of painful stimuli is defective on the left below a line running from about two inches above the nipple to the tip of the left shoulder and then to the spinous process of the third dorsal vertebra. On the right the upper limit is defined by a line across the chest at the level of the lower border of the manubrium sterni; it curves over the top of the shoulder and runs along the root of the neck to the spinous process of the first dorsal vertebra. The analgesia is greatest on the right arm, the right side of chest,

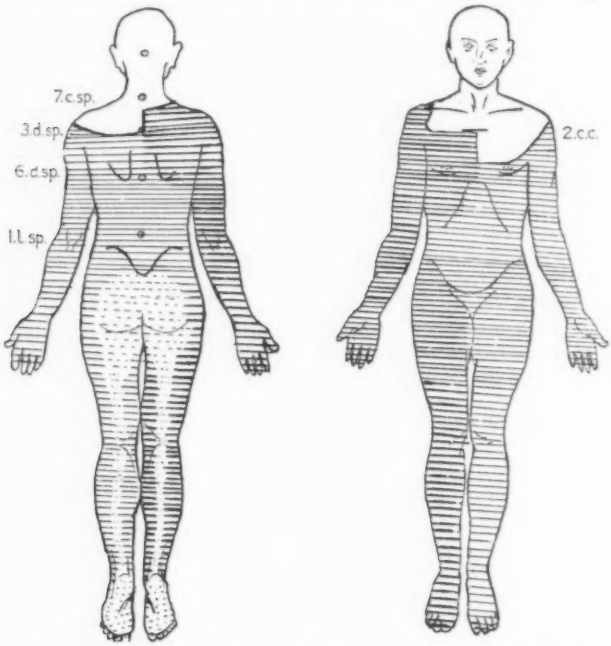

FIG. 2.—Diagram showing impairment of cutaneous pain sensibility. Shaded part indicates area where this is diminished. The degree of shading indicates the degree of impairment.

and the right leg, and least in the area of the sacral roots (fig. 2). Appreciation of heat and cold is impaired up to a slightly higher level (fig. 3). Tactile sensibility is defective below the knees only. The upper limits of the areas of the sensory disturbance do not correspond to root levels or cord segments. Vibration is only feebly appreciated on the styloids and malleoli; on the right malleolus it is hardly perceptible. Postural sensibility is grossly defective in both the upper and lower limbs, especially in the right leg, where even gross passive movements of the toes are not recognized. Two-point discrimination is defective on both palms, and form is not recognized accurately by either hand.

Romberg's sign is marked. His gait is slow and extremely spastic. The feet are just raised off the ground, his steps are short and he walks with a wide base. He is very unsteady and tends to fall forwards. The arms do not swing as he walks.

Nothing abnormal was found in the cardio-vascular, respiratory, alimentary and genito-urinary systems.

The cerebro-spinal fluid was not under pressure and there was no evidence of obstruction. The Wassermann reaction was negative in both his blood and cerebro-spinal fluid.

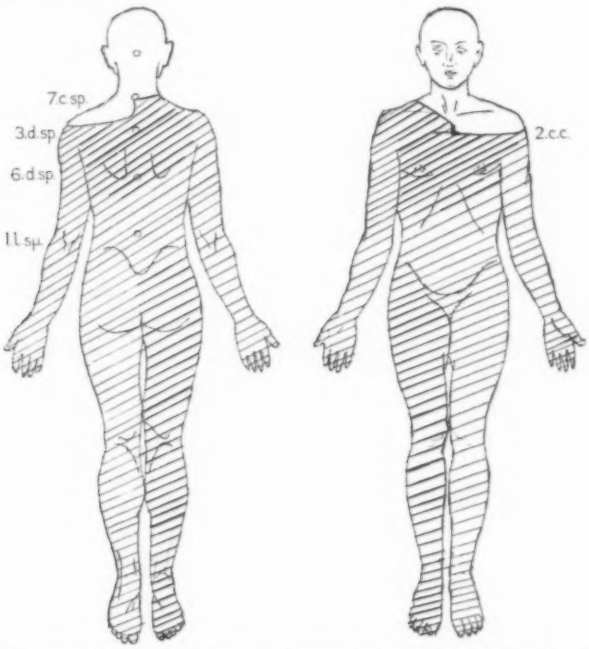

FIG. 3.—Diagram showing impairment of appreciation of heat and cold. Shaded part indicates area where this is defective. The degree of shading indicates the degree of impairment.

Comment.—Attention was first directed to that type of deformity of the shoulder present in my case by Underburg, who, in 1693, reported three cases as dislocation of the scapula. Later, Eulenburg (1863), in Germany, and Willet and Walsham (1880 and 1883) in this country, recorded similar cases. Sprengel [2], in 1891, published three cases, giving a detailed description and making a suggestion as to its ætiology. Since then many other cases have been reported.

The most conspicuous features of the deformity in this patient are

the marked elevation of the left scapula, the shortness of the neck, the tilting of the head and the scoliosis. In the Sprengel deformity the scapula may be normal in size and shape, or may be malformed and irregular. The vertical measurement may be diminished with an increase of the horizontal measurement, causing it to retain a fœtal shape or to approach in form that of the scapula of some of the lower animals, e.g., the sheep. In my case, as in several others recorded [6], [7], [8], a bony bridge, curved, and roughly triangular in shape, runs from the transverse processes of the sixth and seventh cervical vertebræ to articulate at its base with the upper portion of the vertebral border of the scapula. It is probably partly responsible for the fixation of the scapula. Scoliosis, which may be very severe, and defects and anomalies of the ribs, are usually present. In my skiagrams the first three ribs of the left side are very irregular in size and shape, but this may be secondary to the scoliosis of the cervical and upper thoracic spine. Other bony malformations which have been found co-existing with the condition are cleft palate, shortness of the humerus or clavicle, or both, synostosis of the radius and ulna or absence of the radius, maldevelopment of the whole upper limb, club-foot or shortness of the femur [6], [7], [9]. Boyd [10] reported a case in which the deformity was associated with Hirschsprung's disease with intestinal obstruction.

The deformity is a congenital one, and various theories have been advanced to explain its ætiology. Sprengel [2], [9] believed it to be the result of malposition of the fœtus *in utero*. It has been observed that many of the patients were born with posterior displacement of the affected limb. The condition, however, is generally attributed to a developmental arrest. In the early embryo the scapula lies opposite the lower four cervical and the first two dorsal vertebræ. During development it gradually descends, and even at full term it occupies a higher level than it does in later life [9], [11]. Kausch [12], Hödlmoser [13] and Neumann [14] attribute this failure to descend to the abnormality of the trapezius muscle, while Rager [15] suggested that the shape of the superior border of the scapula, and especially the anterior curvature of the suprascapula, may be the cause of the arrest. Chievitz [11] believes the condition to be a reversal to a lower type, or retention in the fœtal position. Others have suggested that poliomyelitis may be a factor (Bloch).

In addition to the deformity originally described by Sprengel, there was in my case abnormality in the conformation of the vertebral column also. Owing to the abnormal position of his head and the shortness of

his neck, it was difficult to obtain satisfactory skiagrams of the upper cervical vertebræ. It was, however, obvious from a series of skiagrams taken from different angles that some of the upper cervical vertebræ were absent. This has been described as the Klippel-Feil syndrome [4] [21], the essential features of which are absence or fusion of some vertebræ, or absence of some with fusion of others, scoliosis, spina bifida and abnormal distribution of the hair of the scalp. Cases have been described in which fusion of cervical vertebræ and malformation of the cranium were associated with ataxia of the Marie and Friedreich types [20].

In this case, therefore, we have two types of skeletal deformity which were originally described separately, but in many of the cases of the Sprengel deformity there have been abnormalities in the development of the vertebral column similar to those in my case and in the one recently described by Macdonald Critchley [1], and also in cases reported by others, e.g., Niederle [3], Fairbank [6] and Hibbs and Correl-Loewenstein [7]. These deformities are evidently congenital in origin and dependent on some anomalies in the development, whatever their immediate cause might be.

There can be little doubt of the nature of the neurological disturbance in my case, as all the symptoms point to syringomyelia. The character of the sensory disturbance, the slow and gradual onset of the condition and the spastic state of the limbs with paresis of the arms, are all in favour of this diagnosis. The negative Wassermann reaction in his blood and cerebro-spinal fluid excludes spinal syphilis, while the absence of any evidence of blockage, as revealed by lumbar puncture, makes a compression of the cord improbable. The possibility of intramedullary tumour has to be considered, but again, because of the absence of evidence of blockage, it is clear that the cord was not sufficiently swollen to obstruct the circulation of the cerebro-spinal fluid.

Syringomyelia is not infrequently associated with other developmental anomalies, and the view is generally held now that in many cases at least the origin of the disease must be sought in some congenital or developmental anomaly of the spinal cord.

A certain amount of importance has been given to trauma in the pathogenesis of syringomyelia [19], but the only injury which the patient received during the years preceding the onset of his symptoms entailed severe bruising of some fingers of his left hand, and this can scarcely have had an influence on the pathogenesis of the spinal disease. The fact that, although the injury was relatively severe, he was able to

continue work, suggests that even at that time there was diminished sensibility to pain in his fingers.

The only case I can find in the literature comparable to my own, in which the Sprengel deformity was associated with syringomyelia, was that recently published by Macdonald Critchley [1], in which, however, the diagnosis has not been confirmed by anatomical examination.

The following is a résumé of the case described by MacDonald Critchley [1].

A man, aged 45, had since the age of 2 years a deformity of the left shoulder and neck and his left arm was weak. At the age of 30 his arms were twisted behind his back, and since then he complained of pain in his thorax and weakness of his legs.

He appeared to have scarcely any neck. The head was tilted towards his left shoulder. The right scapula lay at a higher level than the left and was rotated upwards so that the vertebral border could be felt under the trapezius. There was sharp angular scoliosis of the cervical and upper thoracic vertebræ with the convexity to the right. The angles of the ribs were more prominent on the right side, and the left half of the chest bulged in front. The left arm and leg were smaller than the right and left leg was rigid and longer than the right. The left half of the face was slightly smaller than the right and the palpebral fissures were unequal, but there was no localized wasting of muscles.

Tactile sensibility was undisturbed. The appreciation of pinprick was defective over the whole of the right leg and the right side of the trunk up to the level of the fourth thoracic segment, but the area between the eighth and the fourth thoracic segments was less involved. The appreciation of heat and cold was also impaired over the same area as pinprick. Postural sensibility was defective in the toes and ankles of both feet; vibration was not appreciated on the right external malleolus, and form was not recognized accurately in either hand.

All tendon-jerks were present but exaggerated on the left side, and both plantars were extensor.

The vertebral column appeared to show a reduction in the number of cervical vertebræ.

We may, therefore, assume that we have two conditions usually separate, but both developing on a congenital basis, combined in the case I report here, and in that described by Critchley.

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CHRONIC SUBDURAL HÆMATOMA: A STUDY OF EIGHT CASES WITH SPECIAL REFERENCE TO THE STATE OF THE PUPIL.[1]

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Introduction.

Chronic subdural hæmatoma is diagnosed with sufficient rarity that a review of eight cases, with special emphasis placed on accurate localizing signs, seems worthy of report. Moreover, a correct diagnosis of the site of the lesion should invariably be followed by operation and complete recovery.

A review of the literature of this subject need not be given, for it has been thoroughly covered only recently by Putnam and Cushing [1], and by Sherwood [2].

Six of the eight cases to be reported were personally observed clinically as well as at operation or autopsy, the other two were seen only at autopsy.

That chronic subdural hæmatoma occurs more frequently than middle meningeal hæmorrhage is as yet not fully appreciated. Certainly the syndrome of the former is not as well known. The eight cases to be reported were seen over a period of eighteen months, and during this period one instance of middle meningeal hæmorrhage came to my notice. Only two of the eight cases were correctly diagnosed.

In the study of the cases to follow the clinical syndrome, so clearly described by Trotter [3], has been repeatedly confirmed. Special attention, however, has also been paid to the unilateral dilatation of the pupil which has been found to correspond with the side of the lesion. The sequence of the cases is given in the order they were seen. It will be noted that with the study of each additional case, the clinical picture of chronic subdural hæmatoma became more distinct and more dependable.

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Report of Cases.

Case 1 (Barnes Hospital, Unit No. 222235).—Trauma to occipital region; lucid interval[1] of ten days; headache, drowsiness, pyramidal tract signs pointing to a lesion on the right side. Operation with disclosure of a subdural hæmatoma on the right. Death the following day. Necropsy.

History: W. R., a boxer, aged 27, was admitted to Barnes Hospital on October 27, 1929, complaining of headache and drowsiness.

Ten days previous to his admission he received a blow over the occipital region during a sparring bout which stunned him for a few moments. He was not unconscious. He discontinued boxing and soon started to complain of headache which persisted and kept him awake through the night. His physician found no evidence of intracranial injury at this time. His headaches continued until thirty-six hours before entry, when he became increasingly drowsy and stuporous.

Examination: When first seen at the hospital he could only be aroused to answer "yes" or "no," and would fall back again as if asleep. Both pupils were under the influence of mydriatics. There was a palsy of the oculomotor nerve on the right, as well as a facial weakness of central type on the same side. The fundi were normal. The knee-jerks were more active on the right than on the left. Oppenheim sign was positive on the right, and ankle-clonus was obtained on the left. There were no irritative meningeal phenomena.

The temperature, pulse and urine were normal. The blood-pressure was: systolic 115, and diastolic 70.

Clinical course: The patient was given 50 c.c. of 50 per cent. glucose intravenously with no apparent improvement. Six hours after entry the patient was more stuporous, more difficult to arouse, and the entire left side of the body was spastic with occasional twitchings of the left arm. His pulse dropped from 85 to 64 per minute, and during this time there was a rise of 35 points in systolic blood-pressure. The diagnosis was subdural hæmorrhage on the right side.

Operation: A right subtemporal decompression was done by Dr. Roland Klemme. The dura was tense, greyish-blue, and non-pulsating. As the dura was incised about 100 c.c. of old clotted blood spurted forth. The dura was then opened widely, and about 120 c.c. of thick clotted blood were removed, but no bleeding point could be found.

The following morning the patient was still unconscious. Lumbar puncture yielded 45 c.c. of uniformly blood-tinged fluid. Intravenous glucose was of no avail and he died that afternoon.

[1] By the term "lucid interval," Bowen [4] means the period from the time of trauma to the onset of unconsciousness, and by the term "latent interval" the period from the time of the trauma to the onset of symptoms of intracranial pressure or cortical irritation. These terms will be used in the above sense.

Necropsy: There was no evidence of fracture of the skull. The subdural space on the right was distended with blood, causing several depressions in the brain. The cerebral veins were distended but not thrombosed. There was an area which appeared like an old laceration over the posterior part of the right occipital lobe; the hæmorrhage in part seemed to have come from a vessel deep in that region. The entire right occipital lobe was soft, cyanotic, and covered with blood. There was a marked pressure cone of the cerebellum.

Comment.—A blow over the occipital or frontal region frequently precedes the formation of a subdural hæmatoma. Indeed, it is this type of trauma which shakes the brain in a direction at right angle to the vessels entering the superior longitudinal sinus.

Although headache persisted from the start it was not until nine days following the trauma that drowsiness set in.

Transient signs of left-sided cerebral involvement were soon followed by distinct signs pointing to a lesion over the right motor area.

The findings at operation were typical, and had the patient been spared the additional complication of laceration of the brain with subsequent softening of the occipital lobe, the outcome would unquestionably have been favourable.

In this patient the pupils were under the influence of homatropine before a record of their size and reaction was made, but it will be noted that the third nerve palsy was on the side of the lesion.

Interestingly enough, Brock [5] has recently reported a similar case of chronic subdural hæmatoma in a boxer who had a dilated pupil on the affected side. In this connection it is important to note that since boxing has become a popular sport in Germany, a total number of twenty-two deaths have been reported as a result of injury sustained in the ring. In a study of these cases, Wolf [6] could obtain sufficiently reliable information in thirteen cases only. Of these, 6 or 43 per cent., died of traumatic subdural hæmatoma.

Case 2 (Barnes Hospital, Unit No. 22567).—Head injury followed by unconsciousness for two and a half hours. Latent interval of two months and ten days, followed by headache, disorientation and drowsiness. Pyramidal tract signs on the left. Negative spinal fluid. Death without operation three months after injury. Necropsy disclosure of a subdural hæmatoma on the left side.

History: P. P., an Italian miner, aged 66, entered the hospital on November 20, 1929, complaining of pain over the forehead and over the left temporal region of ten days duration. In September, 1929, while at work in a coal shaft, a large lump of coal struck the left side of his head. He was

unconscious for two and a half hours, then semi-conscious for about another one and a half hours. His condition gradually improved, so that ten days following his injury he returned to work. He continued on his job as a miner for two months and ten days from the date of his injury, when headaches over the left temporal region forced him to bed. His headaches increased in severity and four days before entry he became unsteady in gait and disorientated. Weakness, drowsiness and urinary incontinence soon followed. A radiogram of the skull taken before his hospital admission was reported to have shown a fracture.

Examination: The patient was a frail Italian worker who was confused, disorientated and unable to co-operate. His pupils were equal though the left one was somewhat irregular; both reacted promptly to light. The fundi and the cranial nerves were normal. There was no demonstrable motor weakness and no sensory impairment could be determined. The deep and superficial reflexes were all present, active and equal. There was some rigidity of the neck and bilateral Kernig sign. A positive Oppenheim and a suggestive Gordon sign were found on the left side. The plantar reflexes were normal.

The urine was normal. A lumbar puncture showed clear spinal fluid under normal pressure, containing four leucocytes per cubic millimetre. No organisms were found in the spinal fluid and the Wassermann reaction was negative.

Clinical course: November 24, 1929: A visiting neurologist made the following note. "There is evidence of a lesion of the left hemisphere, which seems to be a receding process and is probably vascular in nature. Babinski is positive on the right. There is a suggestion of astereognosis on the right, although co-operation is poor."

November 27: The patient was confused, disorientated, and soiled himself. On the following day a lumbar puncture was repeated; the fluid was under slightly increased pressure. The cell-count and globulin were normal, the Wassermann and Kahn tests were negative and the colloidal gold was 1122100000.

December 2: The patient's course was steadily downhill. Stupor gradually deepened into coma and he died that night.

Necropsy: A careful search did not reveal any cranial fracture. As the dura over the left hemisphere was reflected there came into view a partially organized blood-clot adherent to the under surface of the dura which covered an area 4 × 5 cm. In addition there were 8 oz. of fairly fresh blood which appeared as if it had recently clotted. Beneath the clot the brain was depressed and yet no great change in the contour of the convolutions was noted. The convolutions of the opposite hemisphere, however, were definitely widened and compressed. Microscopical sections of the brain showed no pathological changes.

Comment.—In this patient there was a "latent interval" of two months and ten days. Once having started, his headaches were followed by disturbed gait, disorientation, drowsiness and periods of unconscious-

ness, all within four days. He appeared tired and sleepy. His malady did not seem serious. Finally, signs of meningeal irritation and inequality of the pupils made luetic meningitis a strong possibility, even in the face of negative spinal fluid findings. With the exception of a positive Babinski on the right and an Oppenheim on the left, no localizing signs were found over a period of twelve days' observation in the hospital. During the intervals when he seemed more alert and responsive there were no suggestions of aphasia.

The findings at autopsy were certainly out of proportion to the scanty neurological signs, thus justifying a feeling of uneasiness about encountering similar conditions in the future. Just one month later another patient came under observation which added more difficulties to our uncertain state of mind about this illness.

Case 3 (Barnes Hospital, Unit No. 2,2887).—Thrown off a horse, unconscious two hours, "latent interval" three weeks. Headaches, drowsiness, stupor, alternating pyramidal tract signs; clear spinal fluid; periods of unconsciousness. No operation; death nine weeks after injury; necropsy disclosed a bilateral subdural hæmatoma.

History: On December 18, 1929, J. S., a physician, aged 60, entered the hospital with the complaint of right-sided headache of seven days duration. He was always a rugged healthy person. On October 24, 1929, his horse stumbled and threw him. When his employees rushed to his aid he asked to be taken to his own home on the premises. Soon he lapsed into unconsciousness which lasted two hours. There was no bleeding from nose, ears or mouth. After three days in bed he began to complain of pain over the lower third of the left tibia. He managed to get about the house on crutches, but complained of increasing pain in his left leg, especially when he shifted his weight to the affected limb. Three weeks after his injury he began to complain of intermittent right-sided headache. Only moderate relief was obtained from increasing doses of "painodyne" tablets. His headaches gradually became more severe, so that by December 8, 1929 (six weeks after his injury) a roentgenogram of his skull was taken which suggested a depressed fracture of the inner table over the left temporo-occipital region. His headaches became more intense, keeping him awake at night, and finally he was brought to the hospital.

Examination: At the time of his admission he appeared well nourished, mentally alert and co-operative. He did not complain very much about his headache. There were no external signs of head injury and no percussion tenderness. The pupils were slightly irregular, equal and reacted promptly to light and accommodation. The fundi were normal. There was a very fine horizontal nystagmus in both directions. The other positive findings were some ecchymosis and tenderness over the injured area of the left leg and

positive Babinski and Oppenheim signs on the right. His condition remained unchanged for the next four days. On December 23, 1929, the patient appeared rather semi-stuporous, the left eye was kept open more than the right. He could be aroused, but when left undisturbed he fell asleep very readily. The abdominal and cremasteric reflexes were absent. The Babinski and Chaddock signs were positive on both sides. A consulting neurologist made the following note: "Nystagmus in both directions, pupils small and equal, lagging of the right side of the face about the mouth, although yesterday the left side of the face seemed to be weaker. Arm reflexes were not obtained, patellar reflex on the right is difficult to obtain, the left one is active. Bilateral Babinski." The spinal fluid was normal.

December 24, 1929: A left peripheral facial weakness was observed. The bilateral Babinski persisted. A medical consultant found the lungs clear although the respirations were of Cheyne-Stokes type. He felt the condition could be accounted for by some intracranial lesion and that it was not due to any general disturbance.

December 25: The patient seemed much brighter after an infusion of 50 c.c. of 50 per cent. glucose. He was able to recognize his nurse, spoke to his relatives, but readily fell asleep when left alone. For the next five days he remained stuporous and did not respond in spite of intravenous glucose therapy at frequent intervals.

December 30: The pupils were pin-point although no narcotics or sedatives were used for five days. Respirations were of the Cheyne-Stokes type. The arms and legs were flaccid.

January 1, 1930: The patient was still stuporous and more difficult to arouse; the new findings were a definite weakness of the right arm and leg and a divergent strabismus on the left.

January 3: Stupor deepened into coma and death ensued. Repeated examinations of the urine were negative except for a trace of sugar following glucose infusions. The blood Wassermann and Kahn tests were negative. The blood-pressure: systolic, 140; diastolic, 100. Non-protein nitrogen 42 mg. per 100 c.c. of blood. Blood-sugar 116 mg. per 100 c.c. of blood. Phthalein excretion was 65 per cent. Roentgenogram of the skull showed no evidence of fracture. The pulse and temperature were normal until close to the end.

Necropsy: The calvarium was removed with ease, and shining through the dura were two greenish-blue masses, one over each hemisphere. As the dura was peeled back the bluish masses were found to be partially organized blood-clots extending over the fronto-parietal-temporal areas and in part adherent to the under surface of the dura. The hæmatoma on the right measured about 5 oz., the one on the left measured 8 oz. The underlying brain was compressed and conformed to the shape of the hæmatoma. The convolutions were not flattened, maintaining their normal configuration. The compression had taken place at the expense of the ventricular system. There was a definite membrane which enclosed these clots and closed them off from the subarachoid space. Many atheromatous plaques were noted over the basilar artery, but

no cerebral thrombosis or laceration could be found. A search failed to reveal any fracture of the skull. On section of the brain there were many small hæmorrhagic areas throughout, and in the middle left portion of the pons there was one large area of fresh hæmorrhage 1 cm. in diameter, undoubtedly a terminal event.

Comment.—Here again there was an interval of three weeks between the time of the injury and the warning sign of headache. That the spinal fluid was normal is not surprising, because a hæmorrhage strictly confined to the subdural space will obviously not stain the spinal fluid. There was no suspicion of aphasia during the entire course of the illness, which can be explained on the basis that the brain makes remarkable adjustments to slowly expanding intracranial lesions.

The clinical picture in this patient varied so from morning to evening, and indeed throughout the entire duration of the illness, that no localization of the lesion could be made with any degree of certainty. The "see-saw" of neurological signs, pointing to one side then to the other, stayed the hand of the surgeon, even to the point of performing a ventriculogram. In retrospect a bilateral trephine over the temporo-parietal region, the most common site of such lesions, would have disclosed both subdural hæmatomata.

With three patients dying of this condition in three months, two undiagnosed until necropsy, it was only natural to be on guard and not to temporize. Before six more weeks had passed such an opportunity presented itself.

Case 4 (Barnes Hospital Unit, No. 23443).—Head injury while under the influence of alcohol. Lucid interval of nine days; ptosis and dilated pupil on the affected side; operation with removal of subdural clot. Recovery.

History: On February 6, 1930, M.W., a coloured female, aged 24, presented herself at the Out-patient Department of the hospital complaining of trouble with her right eye. It was found that she had a complete palsy of the third nerve on the right. The right pupil was larger than the left and fixed to light. She was admitted to the hospital on the eye service.

Her illness started during a drunken spree about nine days previous to entry when she received a blow over the right side of the head and was unconscious for ten or fifteen minutes. That night she had diplopia and the next day she vomited several times. She was troubled very little with headaches, but was concerned about poor vision in her right eye. After eight days in bed she finally came to the hospital.

Examination: In addition to the right amaurosis, a ptosis of the right eye-

lid and sluggish reactions of both pupils to light and accommodation were noted. The remainder of the examination was normal.

Clinical course: The morning following her entry into the hospital she seemed drowsy and by noon she was stuporous. Magnesium sulphate given by rectum did not influence her somnolence. Spinal fluid examination showed a few crenated red cells and seven leucocytes per cubic millimetre. When on the neurosurgical service she could be aroused in spite of her stupor, but her memory seemed to be poor. Several superficial bruises were noted over the left side of the trunk, the left shoulder and the hip. The right pupil remained larger than the left. The blurring of the right optic disc and the fullness and tortuosity of the veins were interpreted as early choking. The abdominal reflexes were diminished on the right. Lues was strongly suspected. On February 10, 1930, Dr. Ernest Sachs made the following note: "This patient presents a very obscure picture, the history is unreliable but there is evidence of trauma. There is a difference between the reflexes on the two sides with a tendency in favour of the involvement of the right pyramidal tract. However, the difference is so slight that more value must be attached to the lesion of the third nerve on the right. The eye grounds are normal. The patient probably has a removable clot and is to have a right subtemporal decompression and if necessary a left one also." The operation was performed by Dr. Roland Klemme. Under local novocain anæsthesia a right subtemporal decompression was performed in the usual manner. As the dura was exposed it was found under great tension, non-pulsating and with the typical blue appearance of underlying encysted blood. The dura was carefully incised and a large hæmorrhagic cyst came into view. This extended over the right cerebrum as far as could be seen with the exposure that was made. The hæmorrhagic fluid was sucked out, the clot and most of the membrane that was within reach were removed. The brain did not expand as it was expected, although it pulsated normally. No bleeding point could be discovered. The dura was not sutured and closure of the wound was performed in the usual manner except that a gutta-percha drain was inserted in order to guard against the possibility of further bleeding. While on the operating table, the patient had awakened and seemed alert, orientated and co-operative. However, about seven hours later, she developed restlessness, seemed to be less alert and was somnolent.

The next morning she was comatose and the right side of her body was much weaker than the left. There was no drainage from the wound when the patient was placed on the operating table with head lowered for the purpose of re-exploring the wound. The removal of the drain was followed by the escape of about 4 oz. of bloody fluid. The patient aroused immediately, regained consciousness, and after a short interval was returned to the ward.

February 12, 1930: There was abundant drainage on the dressing. The temperature was 40·4° C. She appeared more comfortable and more alert after an ice pack. Ptosis was less marked on the right.

February 13: Palsy of the third nerve on the right was definitely clearing.

February 15: Although the temperature was normal the patient presented

signs of mild meningeal irritation. This was believed to be the result of the presence of blood in the subarachnoid space.

February 17: The palsy of the third nerve on the right had completely cleared and the signs of meningeal irritation had disappeared.

February 21: The patient appeared quite sick and had fever. Twice that afternoon she vomited. There were no abnormal neurological signs. Two days later she complained of pain over her right chest and respirations became more laboured and more rapid. Signs of an abscess of the lung were found on the right, this being confirmed by roentgen ray examination. Postural drainage was instituted and continued until all of her signs cleared up.

The head wound healed by primary union, the decompression pulsated freely. She was discharged from the hospital cured on April 15, 1930, nine weeks after her admission.

Comment.—In this patient the history of injury to the head was not certain, but the slight bruises over the trunk led us to suspect the possibility of an injury to the skull.

Not infrequently a paralysis of the third nerve occurs in instances of aneurysm at the point of bifurcation of the internal carotid and in meningo-vascular syphilis. But the unexpected onset of unconsciousness and the normal spinal fluid made these unlikely. The dilated and fixed pupil on the right was in conflict with the homolateral pyramidal tract signs, but corresponded with the side of the lesion. Had we taken the attitude indicated in Dr. Sachs' note, in some of our preceding cases or in those to be reported, more recoveries would have followed. It was difficult to explain the comatose state of the patient and the weakness of the right side of her body which occurred on the morning following the operation, for it has been the consistent experience of neuro-surgeons that subdural bleeding practically never recurs once the clot has been removed. It is very likely that the state of unconsciousness which occurred on the morning following the operation resulted from the accumulation of cerebro-spinal fluid which had replaced the hæmatoma, for when this was allowed to escape consciousness promptly returned. A similar sequence of events occurred in another patient who had an extradural hæmorrhage with a tear of the dura. She regained consciousness on the operating table, but on the following morning stupor set in which cleared up shortly after the removal of the drain with the escape of bloody fluid on the dressing.

Case 5 (Bellevue Hospital).—Latent interval of one month; headache, vomiting, stupor, a dilated pupil on the left. Tumour of the brain suspected, no operation, necropsy with disclosure of a subdural hæmatoma on the left.

History: M. D., a divorced woman, aged 35, was brought to the hospital on October 3, 1930, in a comatose state. One month previously she was brought to the psychopathic ward and was discharged immediately as "not a proper case." No record of her condition at that time could be found. According to a friend she was perfectly well until four days before entry when she complained of headache and had projectile vomiting but no convulsions or visual disturbances. She had not taken any drugs or alcohol. On the morning of entry when her friend left her she seemed to be well except for her headache.

Examination: The patient was in coma, breathing regularly and deeply. She gritted her teeth continuously and was not inclined to move her left arm and left leg. There was profuse salivation. No characteristic odour to the breath could be detected. There were some traces of old ecchymosis about the right eye. The left pupil was larger than the right, both reacted sluggishly to light, and a mild external strabismus was noted on the left. The fundi were normal. The left arm was flaccid and the deep reflexes in that extremity could be elicited with considerable difficulty. The left leg moved under painful stimulation. The right abdominal reflex was diminished. The Babinski sign was positive on both sides. The urine showed a heavy trace of albumin. Blood-pressure: systolic 140, diastolic 90. Blood-sugar 120, N.P.N. 30. Only about 1 c.c. of spinal fluid was removed, for it was found to be under increased pressure. It appeared clear and colourless, but microscopically showed numerous red blood-cells and six white cells.

Clinical course: The patient was given 200 c.c. of 25 per cent. glucose intravenously. A lumbar puncture was repeated and showed a clear fluid under markedly increased pressure. The globulin and the sugar were normal. There were 120 leucocytes, 90 per cent. of which were mononuclear cells.

October 4, 1930: The patient was still comatose. There were signs of meningeal irritation. Under painful stimuli the left arm would move slightly. Abdominal reflexes were not elicited. Intravenous injection of 200 c.c. of 25 per cent. glucose was given and repeated that evening with no apparent improvement.

A neurological consultant found both pupils under the influence of homatropine. The fundi were normal, breathing was of the Cheyne-Stokes type and she was able to move all her limbs equally well. Bilateral Babinski signs were present but more marked on the left. The impression at this time was that we were dealing with a case of meningo-vascular syphilis.

October 5: At this time, because of the use of homatropine, the right pupil appeared larger than the left, both being fixed to light. There were no motor disturbances.

October 6: The temperature rose to 108° F., the respirations were 52 and the pulse was 170. The patient remained in coma and died on that day.

Necropsy: There was ecchymosis about the right eye. The right pupil was larger than the left. Three superficial bruises were found over the left arm and leg. The calvarium was removed with ease, and over the left hemisphere there was a greenish blue mass shining through the dura. As the dura was elevated

there came into view a large flabby clot weighing about 150 grm. and covering almost the entire left hemisphere. The clot was encased in a thin fibrous membrane and only a small portion of it was liquefied. The remainder of the clot had the consistency of "wet blotting-paper." The underlying cortex appeared normal, but the cerebral cortex on the right was œdematous, and the convolutions were compressed and flattened. There was no evidence of a fractured skull.

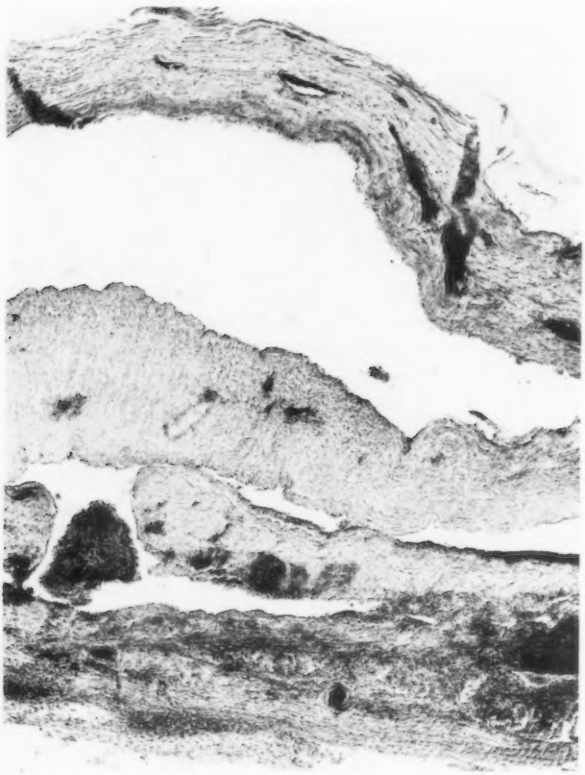

FIG. 1.

Microscopical sections from the region of the hæmatoma show outgrowths of many varying sized small vessels from the inner layer of the dura (fig. 1) which are accompanied by fibroblasts. This has the appearance of granulation tissue. There is a thicker layer of fibrous tissue nearest the under surface of the dura which is a continuation of the membrane that encased the clot. The latter can be best seen at the point of juncture of dura and clot. Sections from

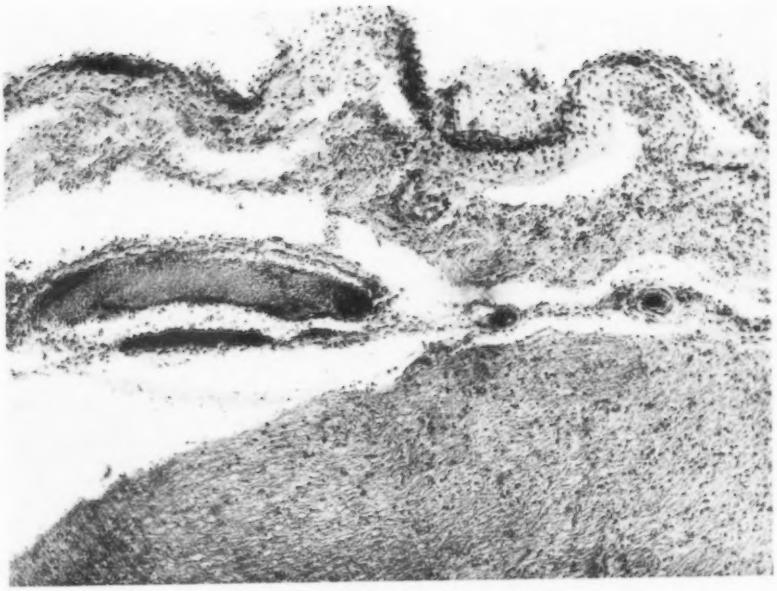

FIG. 2.

FIG. 3.

the brain underlying the clot (fig. 2) show that the subarachnoid space is compressed, and from its outer surface there is a hyperplasia of a mesothelial layer of cells which forms the inner portion of the cyst wall or neo-membrane.

Comment.—This patient presented a most difficult problem in diagnosis. The examination of the urine, blood and spinal fluid did not give any clue. There were, however, external evidences of trauma. It seems reasonably certain that her temporary admission to the psychopathic ward one month previously was not accidental and actually marks the onset of her illness. I believe she had a latent interval of one month, for the hæmatoma showed sufficient organization for a process of long standing. Again it should be noted that there were no manifestations of aphasia in spite of an extensive clot overlying the left hemisphere.

The dilated pupil on the left, observed at the time of entry, corresponded with the side of the lesion. Subsequent observations of the state of the pupils were misleading, for they were under the influence of mydriatics. The few pyramidal tract signs which were elicited were misleading, for they were homolateral to the side of the lesion. The possible causes for such misleading signs will be taken up later in greater detail.

The gross and microscopic findings are similar to those found in some of the previous cases and are in agreement with the findings of other observers who have described this type of lesion.

Case 6 (Bellevue Hospital).—Injury to the occipital region during an alcoholic state; headache, vomiting and drowsiness; lucid interval of four days. Right pupil larger than left, normal fundi. Pyramidal tract signs pointing to a lesion on the left; alternating periods of drowsiness and alertness, subsequent appearance of papillœdema. Negative exploration on the left. Death. Necropsy: disclosure of a subdural hæmatoma on the right.

History: On November 5, 1930, a 23-year old clerk entered the hospital complaining of pain over the occipital region and drowsiness.

Four days before entry when he returned home after a drinking bout he struck the back of his head against the wall. This was followed by unconciousness for about five or ten minutes and shortly afterwards by vomiting. He slept well that night but upon arising he experienced severe occipital headaches which, in addition to his drowsiness and vomiting, continued up to the time of admission

Examination: He appeared lethargic and acutely ill, complaining of severe frontal headaches. There was a tender bruised area over the left occipital region. Both pupils reacted to light but not on accommodation. The right pupil was larger than the left and there was considerable difficulty in convergence. The fundi were normal. There was slight rigidity of the neck but no

Kernig sign. Plantar stimulation produced fanning of the toes on the right but no Babinski phenomena. The urine was normal. Blood-pressure: systolic, 140; diastolic, 110; white blood-cells, 16,350 per cubic millimetre, with 83 per cent. polynuclear cells. The spinal fluid was uniformly bloody and under normal pressure.

Clinical course: That evening the patient could be aroused to answer questions. The pulse gradually became slower and the systolic pressure mounted 20 points. There was a supranuclear right facial weakness, the right grip was weaker than the left and the right knee-jerk could not be elicited. He was given 100 c.c. of 50 per cent. glucose intravenously. Two hours later his blood-pressure was 115 systolic and 100 diastolic, respirations were 16 per minute and he was less drowsy. After another hour, when aroused, he expressed the desire to go home.

Neurological examination showed in addition an internal squint of the right eye and beginning papillœdema.

Because of his restlessness he was given magnesium sulphate (25 per cent.) by rectum. About midnight the right side of his body became more spastic.

On the following morning his mental state and general condition were much improved, but three hours later he again became stuporous, his pulse became slow and his papillœdema had advanced. His pupils were under the influence of a mydriatic. The lower right facial weakness was more definite, the right arm weaker and no sensory changes could be made out. It was believed that he had a subdural or epidural hæmorrhage over the left motor area.

Operation: A subtemporal decompression was performed on the left. The dura was tense and the brain was under considerably increased intracranial pressure, but no extradural or subdural hæmorrhage was found.

The morning after operation his papillœdema was more marked, his pulse rose from 60 to 128 per minute and he had Cheyne-Stokes type of respiration. The right fundus showed choking of 4 diopters and the left 3 diopters. He gradually became more restless and more difficult to arouse. A lumbar puncture was repeated and again showed a uniformly bloody fluid. Four hours later the patient was mentally clear, orientated and spoke rationally. The right facial weakness noted in the morning was absent.

November 8: The patient was rational, fairly alert, quiet and in general appeared to be doing well. However, his papillœdema was advancing.

Second operation: An osteoplastic craniotomy was performed on the left. The dura was under great tension but no extradural or subdural pathology was found. He died the following morning.

Necropsy: This was restricted to the head. As the calvarium was removed the dura was found to be extremely tense. There was no unusual change at the site of the operation, but shining through the dura on the right side a subdural clot was seen. When the dura was opened about 50 c.c. of bloody fluid escaped and there remained about 60 c.c. of a blood-clot which was easily removed. The brain showed several deep contre-

coup lacerations on the right side. About the lacerated areas, which in places were ¾ in. in depth, and underneath the arachnoid there was considerable hæmorrhage. The left hemisphere was œdematous and showed marked convolutional flattening. Microscopical sections failed to show any other lesions except that of local hæmorrhage and œdema.

The base of the skull showed an extensive fracture beginning in the left occipital region, running along the suture line between the left parietal and occipital bones and continuing on the other side of the foramen magnum to the lower portion of the right parietal bone and ending in the squamous portion of the right temporal bone.

Comment.—The history of this patient in many respects resembles those reported above; namely trauma to the occipital region, headache, drowsiness, stupor, intermingled with periods of surprising mental alertness. It is remarkable that following the severe skull injury he was able to get about, being as active as usual. It was only upon the urgent advice of his physician that he finally came to the hospital. From his appearance, his drowsiness and stupor closely resembled natural sleep. At times his drowsiness was not unlike that of patients who have been treated with morphine.

The pyramidal tract signs again pointed to the wrong side of the lesion, but the pupil, so often disregarded, at the very outset indicated the site of the trouble. Bloody spinal fluid may mean that we have, as was found in Case 1, additional cerebral laceration, or that there is a communication between hæmatoma and the subarachnoid space.

Case 7 (Bellevue Hospital).—Comatose state. Right pupil larger than left; questionable localizing pyramidal tract signs; bloody spinal fluid, choked discs. Death without operation. Necropsy revealed a subdural hæmatoma on the right.

History. On November 4, 1930, D. S., a 63-year-old Irish labourer, found lying on the pavement in coma, was brought to the hospital. No history could be obtained.

Examination: There were no signs of any scalp wound or bleeding from any of the orifices. He had some minor lacerations of his lips but no areas of ecchymosis. The right pupil was larger than the left and both reacted promptly to light. In the evening he seemed to be sleeping quietly and perspiring profusely. There were occasional movements of the arms. The urine was normal and blood-pressure was systolic 130, diastolic 70. White blood cells numbered 16,500 per cm. Spinal fluid was uniformly bloody.

Clinical course: The next day he was mentally clear and co-operative. The right disc margins were hazy, the left arm and leg failed to respond to pin-prick and the abdominal and deep reflexes could not be elicited.

November 6: The patient kept mumbling to himself and was irrational. Roentgen ray of the skull showed no evidence of fracture.

November 7: The patient was well orientated and mentally clear, but toward the latter part of the morning he presented the picture of alcoholic delirium. Several hours later he was conscious and answered questions satisfactorily. Both pupils reacted sluggishly to light and the right disc margin still appeared hazy. The Babinski sign was negative.

November 11: The spinal fluid had an icteric tint, but contained no red blood cells.

November 14: The patient was again comatose, his pupils were dilated as a result of homatropine and both disc margins appeared blurred, the right more than the left. There was a right central facial weakness. In addition to a flaccidity of the upper right arm there was spasticity of the left arm and leg. The deep reflexes on the left were over-active. The signs and symptoms pointed to a pachymeningitis hemorrhagica interna. When seen that afternoon the patient could not be aroused, the right disc margin was hazy and the veins were markedly engorged. The right facial weakness was questionable at this time. There was a coarse tremor of both hands but no Babinski sign.

In the evening his coma deepened, the right facial weakness became more distinct, the left side of the body more spastic and the deep reflexes of the left upper extremity more active. There was a positive Babinski sign and ankle clonus on the left, but the patellar responses could not be elicited.

November 16: The fundi showed bilateral papillœdema of 3 diopters. A clear slightly xanthochromic fluid under increased pressure was obtained by lumbar puncture. Hypertonic glucose solution was given intravenously without noticeable effect.

November 19: In spite of repeated intravenous injections of hypertonic glucose solution and repeated lumbar punctures his coma deepened. His papillœdema advanced to an elevation of five diopters. The pulse, temperature and respirations all mounted, and after a stay of fifteen days in the hospital he died.

Necropsy: Externally there was no evidence of violence. The scalp was removed with ease and did not show any subcutaneous hæmatoma. When the calvarium was removed it exposed a tense dura, and over the right hemisphere a dark bluish mass could be seen shining through. As the dura was incised there spurted forth about 60 c.c. of recently clotted blood. However, a flat laminated blood-clot remained adherent to the under surface of the dura. When this was removed several pigmented and bleeding areas, having the appearance of granulation tissue, were visible.

The brain showed no laceration or sclerotic changes. The hæmatoma indented the right hemisphere, making a kind of bed for itself, being enclosed in a fine neo-membrane which stripped easily from the arachnoid. The base and vault of the skull showed no fracture.

Comment.—As in the previous patients, in this case we also had alternating periods of stupor, consciousness and coma, varying from

several hours to several days. The pyramidal tract signs pointed to a lesion over the right motor area, but because they were not consistent, and because the facial weakness was not in keeping with the other signs, one hesitated in making a localizing diagnosis. The right pupil, however, was larger than the left and corresponded with the side of the lesion.

In view of the necropsy findings in Case 6 it was natural to suspect that in this case too one was dealing with a similar process. But unfortunately the sad experience of being misled by the pyramidal tract signs in the previous case prevented a similar undertaking. The necropsy findings were similar to those found in Case 6 with the exception that the brain and the skull revealed no abnormality.

Case 8 (City Hospital). Blow over the head during a drunken brawl; latent interval of one week; ptosis of the right eyelid ten days after the injury. Right pupil larger than left, indefinite pyramidal tract signs, diagnosed as acute encephalitis. Death. Necropsy disclosure of a subdural hæmatoma over the right hemisphere.

History: J.G., a porter, aged 45, entered the hospital on December 4, 1930, complaining of soreness all over the body, especially between the shoulders, generalized weakness, headache, ptosis of the right eyelid, and a watery discharge from the right eye. Twenty years previously he sustained a fractured skull, followed by complete recovery.

It was learned from his wife that for two weeks he had been drinking heavily, and that during one of his "drunks" he either fell or was in a fight, and received several severe blows over the head and body.

For a week previous to his admission he complained of fronto-occipital headaches, and on several occasions, usually in the morning, vomited forcefully. Ptosis of the right eyelid came on suddenly four days before entry, this being accompanied by a watery discharge from the eye.

Examination: On admission he was lying quietly in bed, but was rather drowsy. There were some abrasions over the right eye and forehead, and a hæmatoma over the right frontal region. An old scar about 1 in. long was found over the left occipital region. There was a ptosis of the right eyelid and the conjunctiva on that side was injected. The right pupil was larger than the left, and both reacted to light and accommodation. The fundi were normal. The deep reflexes were exaggerated; a Babinski sign on the right was equivocal, and ankle clonus was poorly sustained on the same side. The urine was negative, white blood-cells numbered 9,000 per c.mm. The blood Wassermann and Kahn tests were negative. On two different occasions the blood-urea nitrogen was 21 mg. and 18 mg. per 100 c.c. of blood. A Roentgen ray of the skull revealed an old oval defect over the region of the lambda.

Clinical course. December 8, 1930: The patient was sleeping most of the time and perspiring profusely. When aroused, he seemed dull and listless. From time to time he tried to get out of bed. Lumbar puncture that morning showed clear spinal fluid, four lymphocytes, no globulin, and a trace of sugar. The Wassermann and Kahn reaction and culture of the spinal fluid were all reported negative. The colloidal gold curve was 0011111100. Toward the evening he became more lethargic; had a coarse tremor of all the extremities and manifested generalized muscular spasticity. It was thought that he had acute encephalitis. Cisternal puncture was done and the fluid was found to be under slightly increased pressure, but otherwise normal.

December 10: He was given 250 c.c. of 25 per cent. glucose intravenously, which had no effect on his lethargic state. Next day the temperature rose to 102° F., and he became incontinent. The following day he was very weak, dull, perspiring greatly, and taking very little nourishment. His temperature rose to 105·2° F., and he died.

Necropsy: When the calvarium was removed it became evident that there was a subdural hæmatoma on the right. The outer surface of the dura appeared pigmented, and there were some golden specks over the involved area. After the removal of about 100 c.c. of dark red clotted blood from underneath the dura, there came into view some firm dark-red clots which were adherent to the under surface of the dura and could be shelled off fairly easily. The clot ended abruptly, and a fine membrane could be seen running from the edge of the clot to the arachnoid. The arachnoid over the right hemisphere was reddish, and over the outer surface of the occipital region was a small dark area which appeared like a ruptured vein. The right hemisphere was somewhat smaller than the left, and the cortical convolutions of the left hemisphere were flattened. There was also a diffusion of blood underneath the arachnoid of the left parietal region.

On section the brain showed no lesions. Except for an old healed fracture over the left occipital region the skull was perfectly normal.

Comment.—The history and sequence of events in this case, with the exception of a previous operation, is almost identical with Case 4. In both there was a head injury during an alcoholic spree, an interval of ten days with headache and vomiting, followed by a sudden onset of an oculomotor paralysis on the affected side, drowsiness and coma. Fluid obtained from the lumbar region and also from the cisterna magna gave no indication of the intracranial hæmorrhage and again the fundi failed to show evidence of increased intracranial tension. That the patient was thought to have acute encephalitis is not surprising, for indeed it closely simulates chronic subdural hæmatoma, with but one exception, a history of trauma.

It is noteworthy, however, that the ptosis and the dilated pupil corresponded with the side of the lesion.

Summary of Cases.

Analysis of the cases brings out several interesting and instructive features about chronic subdural hæmatoma. The ages in this small group varied from 23 to 66 years, the average being 43 years. This condition, however, occurs not only in adults but also in infants, most frequently during their first year of life, as was shown by Sherwood [2].

There were six males and two females. The lesion was unilateral in seven cases and bilateral in one. All had either a history or evidence of trauma, or both. The interval from the trauma to the onset of the first symptom varied considerably. In Case 1 the patient complained of headaches immediately following the blow on the head, while in Case 2 the patient remained free from symptoms for two months and ten days, during which time he was able to carry on his work as a miner. The most prominent symptoms during the lucid interval were headache, drowsiness and vomiting. Objectively, lethargy resembling natural sleep and the alternating periods of alertness and somnolence were most characteristic.

In five of the eight cases the fundi were normal throughout the entire course of the illness; in one the disc margin was hazy on the affected side and in two instances changes in the fundi progressed to advanced papillœdema. The spinal fluid was perfectly clear and normal in five cases and bloody in two cases. In one case (Case 1) lumbar puncture was not done previous to operation. In five cases the pyramidal tract signs were misleading, indicating the wrong side of the lesion; in two instances they fitted in with the other findings and indicated the correct side, and in the patient who had alternating pyramidal tract signs, necropsy showed bilateral subdural hæmatoma. Only one patient had a fractured skull. In all the cases laboratory studies of the urine, Wassermann and blood were normal. In four instances there was a history of alcoholism.

The correct interpretation of the pupillary changes would have been most valuable, for in five cases a dilated pupil was found on the affected side and in one patient a third-nerve palsy was observed on the side corresponding with the lesion, but no note was made about the size of the pupils. In two cases there was a slight irregularity of the pupils but no inequality. One of these patients had bilateral subdural hæmatoma.

Only three patients were subjected to operation and of these one recovered. In another, the diagnosis was correct but the patient had

additional laceration of the brain, and in the third the lesion was wrongly localized. Those who were not subjected to operation died.

Anatomical considerations.—The relationships of the subdural space are well known. Under normal conditions this space is only a potential one. It is enclosed by the under surface of the dura and the outer layer of the arachnoid, contains no fluid and is lubricated by the moisture of its two enclosing surfaces. The subdural space does not communicate with the arachnoid space and as far as is known has no absorbing power. Cerebral veins, being relatively fixed at the superior longitudinal sinus and cerebral cortex, are least supported in their course through the subdural space. Suspended within the skull by various folds of dura the brain has its greatest play in the antero-posterior direction and practically no play in a lateral direction. These anatomical considerations will help explain some of the processes that take place.

Etiological factors.—Since the description in 1857 by Virchow [7] [16] of the condition which he named Pachymeningitis hemorrhagica interna, there has been considerable controversy as to its ætiology and mechanism. With minor variations the findings in chronic subdural hæmatoma are identical with those found in pachymeningitis interna. Virchow put forth the theory that in the insane, in chronic alcoholics, and at times in syphilitics, the dura becomes chronically inflamed, as a result of which there is a pouring out of fibrin and blood-tinged fluid on its under surface. In an attempt to organize this exudative material numerous capillaries sprout from the under surface of the dura with the formation of a granulating surface. When the original circumstances that led to the previous bleeding repeat themselves, or possibly without obvious cause, spontaneous successive bleeding occurs from this surface. The hæmorrhage in turn becomes organized, with the formation of various laminated layers of healed granulation tissue.

Virchow's view of the ætiology of this condition did not remain unchallenged, and since then numerous attempts by various workers, Kremiansky [8], Kassemeyer [9], Rosenberg [10] and others, were directed in search of the direct cause. Notably among these workers has been Barret [11], who carried out under most aseptic precautions bacteriological studies in twenty-three such cases and with one exception, probably an accidental contamination, the results were invariably negative. In eight instances, under aseptic conditions he transplanted portions of the subdural membrane into the subdural space of cats and

dogs with entirely negative results as far as the production of a progressive hæmorrhagic process comparable to that occurring in man was concerned. Various chemical studies did not offer a satisfactory explanation. Those who held Virchow's view that pachymeningitis hæmorrhagica interna was the result of a generalized disease process had difficulty in explaining the localized nature of the lesions, the predilection for areas over the cerebral hemispheres, and the proximity of the lesion to the superior longitudinal sinus. Recently trauma as an ætiological factor has received experimental as well as clinical confirmation.

In 1872 Sperling [12] injected blood into the subdural space of dogs and found that organization began within a week and that membrane formation was found after three weeks. He then carried out similar experiments, using defibrinated blood, and did not find any membrane formation, which led him to the conclusion that organization was the result of fibrin irritating the dura. Microscopically the findings corresponded in all points with those found in pachymeningitis hæmorrhagica interna as originally described by Virchow. He then injected various irritating substances, such as dilute solutions of tincture of iodine, sodium chloride and acetic acid, into the subdural space and obtained negative results.

A similar series of experiments were reported by Spiller [13] in 1899. By nicking the superior longitudinal sinus in cats and dogs sufficiently to produce subdural hæmorrhage and by sacrificing the animals at intervals from six hours to five weeks, he was able to study the various steps in the formation of chronic subdural hæmatoma. He came to the following conclusions: (1) that evidence of new membrane formation was quite distinct after five days; (2) that organization begins nearest the dura; (3) that after five weeks the membrane is distinctly formed; and (4) that subdural hæmorrhage may be one of the causes of the formation of a subdural membrane. Experiments in which he painted the under surface of the dura with hydrochloric acid showed no evidence of membrane formation even after seven weeks.

In a recent analysis of forty-two cases of chronic subdural hæmatoma collected from the literature, Jelsma [14] found that only 2 per cent. failed to give a history of trauma. Indeed, the injury to the head may be so trivial that the patient fails to mention it, and in some instances the story of a head injury is first elicited after operation. In only 25 per cent. of these cases was the injury sufficient to produce unconsciousness. Of the eight cases in this review, seven had a definite injury to the head, and although in one case a history of injury could

not be ascertained it seemed very probable. Unconsciousness following the injury was questionable in 50 per cent. of the cases, in the remaining it varied from five minutes to two and a half hours.

One is inclined to agree with Trotter [3] that the rôle played by trauma in the formation of chronic subdural hæmatoma is often discounted, particularly so in individuals found in insane asylums, in those who are under the influence of alcohol, and in luetics with mental changes.

The notable increase in the number of reported cases of chronic subdural hæmatoma in Germany since boxing has become so popular points very strikingly toward trauma as the ætiological factor.

It would seem then from the above studies that chronic subdural hæmatoma is a result of trauma to the head which displaces the brain in an antero-posterior direction with a resulting tear of one or more of the cerebral veins as they enter the superior longitudinal sinus and with subsequent bleeding into the subdural space.

The Pathology.

The hæmatoma is larger in the antero-posterior diameter and may vary greatly in size, extent and consistency. In over 50 per cent. of the cases the hæmatoma contains liquefied material having the appearance of blood-stained serum. The main part of the clot has the consistency of wet blotting-paper, but the portion of the clot nearest the under surface of the dura is more tense, strips with difficulty and after its removal exposes a reddish granulating area which bleeds easily. With two possible exceptions all reported cases of chronic subdural hæmatoma have been confined to the cerebral hemispheres [15].

Microscopically (figs. 1, 2 and 3) small capillaries are found anastomosing with each other, supported by a connective tissue framework which becomes thick as it approaches the dura. The walls of the vessels are rather thin and friable and in places consist only of large blood-containing spaces lined by endothelial cells. These spaces arise from the inner and more vascular part of the dura in an effort to organize the blood-clot. There are no blood-vessels in the arachnoid, and the only response made by this structure is a proliferation of a thin layer of mesothelial cells. It seems reasonably certain that the clot comes first and the organizing process is a response on the part of the under surface of the dura.

The bleeding in chronic subdural hæmatoma is from a venous

channel and is therefore slow, intermittent and variable. Invariably the rupture is in a vein entering the superior longitudinal sinus and the oozing that follows slowly dissects its way in the subdural space and if strictly confined to this space will not give any evidence of hæmorrhage in the spinal fluid. A small tear in the arachnoid will allow the escape of blood into the subarachnoid space, but this leak may soon seal itself and the fluid obtained from the spinal canal may be first xanthochromic, then clear and finally normal. The hæmatoma forming slowly over a period of days, weeks and months, acts like a growing sponge, displacing the brain tissue slowly and making a bed for itself [17]. The cerebral hemisphere on the side of the hæmatoma is smaller and usually compressed downward and inward. The opposite hemisphere is as a rule larger, more œdematous, and because it is pressed against the resisting cranial vault the convolutions become flattened and widened. The ventricular system is displaced away from the lesion and results in distortion of the size and shape of both ventricles.

Oozing from a cerebral vein will be favoured by variations in intracranial pressure, especially when that pressure falls as a result of dehydrating measures. When, however, the cyst wall has fully formed and hæmorrhage takes place within the cyst, the increased tension in the non-yielding structure will cause headache, vomiting and drowsiness. As the clot retracts and partial organization takes place, the intracranial tension readjusts itself and the patient becomes more alert and at times fully orientated. With the recurrence of the hæmorrhage the stupor and coma return.

That bilateral hæmatoma occurs in one-half to one-third of all cases, as believed by Trotter [3], is not so certain. Of ten cases reported by Cushing and Putnam only one had bilateral hæmatoma; in the series of forty-two cases by Jelsma [14], which included the above number, only two had the lesion on both sides. In all of the seven cases reported by Rand [18], the lesion was found to be unilateral. Among the eight cases reported here, bilateral hæmatoma occurred only once. The incidence of bilateral subdural hæmatoma is probably closer to 10 per cent.

For this reason it is important to localize the side of the lesion, keeping in mind, however, that such may be found on both sides, but not as frequently as previously supposed. Close observation of the changing state of the pupils in these patients will yield valuable information as to side involved.

The Pupils.

There still is variance of opinion about the pupillary changes in patients with cerebral injuries. This is not surprising when we realize that the size and the response of the pupils change frequently following trauma to the head. A careful study of Macewen's article [19] will enable one to understand better the pupillary signs during various states of shock and more particularly in head injuries. This article clearly illustrates that the size and the response of the pupil depends upon the degree of pressure which inhibits cerebral function.

Macewen tabulates the phenomena observed in his case into four phases, which are dependent upon the degree of functional disturbance of the cerebrum.

Pressure	Action on the brain	Effect on the pupil
1. Very severe	Function almost in abeyance ..	Stabile mydriasis
2. Removal of pressure ..	Restoration of function ..	Normal and active
3. Slight	Interruption of function ..	Contracted and sluggish
4. Very severe	Suspending of function ending in abolition ..	Stabile mydriasis

We see then that pupillary changes particularly in head injuries are transitory and only by careful and repeated observations will reliable and dependable information be forthcoming. During the irritative state, when one half of the cerebrum has had its functions interfered with, the pupil on the side of the lesion may well be smaller than on the non-affected side, but when the function of one half of the cerebrum is totally suspended then the pupil on the affected side is dilated and fixed.

From the study of the eight cases it would seem very likely that the third nerve in its course may easily be influenced by variations in intracranial pressure, as a result of which frequent pupillary changes are encountered. This nerve is likely to suffer from pressure as it crosses the sharp edge of the greater wing of the sphenoid. Pressure transmitted downward and inward, as is so often the case in subdural hæmatoma, will readily affect the behaviour by influencing the activity of the third nerve. Ptosis of the eyelid accompanying the dilated pupil would argue in favour of such a mechanism. During the early phase pressure will cause irritation of the third nerve and will result in a small pupil on the corresponding side; the pupil on the opposite side, however, will be normal in size and respond promptly to light and accommodation.

Pupillary changes give evidence of increasing pressure in cerebral

trauma long before the appearance of papillœdema. In a good number of instances of cerebral trauma the dilated pupil may be the only localizing sign. As has been pointed out by Holman and Scott [20], and by Rand [21], the dilated pupil is of greater significance than a hemiparesis or bleeding from the opposite ear. That a hemiparesis has led to a negative exploration has been the experience of many neurosurgeons. In some cases one is unable to assign any cause for such misleading signs.

Misleading Pyramidal Tract Signs.

The finding of a lesion on the side homolateral with the disturbed pyramidal tract signs suggests that there was either an error in observation or a fault in interpretation. The explanation for this inconsistency is rather to be found in the morbid changes affecting the nervous system.

Misleading pyramidal tract signs have been accounted for in three ways.

(1) A study by Kernohan and Woltman [22] has shown that in those instances in which the pyramidal tract signs were misleading a distinct notch was found in the crus on the side contralateral to the lesion, at the point where it impinges against the incisura tentorii, thereby giving homolateral pyramidal tract disturbances.

(2) Then again such misleading signs have been attributed to the dilatation of the lateral ventricle on the side opposite the lesion. This can hardly be accepted for unilateral dilatation of a lateral ventricle is of frequent pathological occurrence, yet it is sometimes associated with pyramidal tract disturbances as a result of such dilatation.

(3) Finally, the most plausible explanation is that in the gradual and slow formation of the hæmatoma the underlying cerebral substance is steadily pushed away from the side of the lesion. The affected hemisphere is shrunken, but the convolutions still maintain their normal configuration. The opposite hemisphere on the other hand is much larger, more œdematous, and the convolutions flattened and compressed. Such findings have been consistent in five of the cases reported here which exhibited misleading pyramidal tract signs. Similar observations were also made by Vance [23]. It would appear then that the motor area of the cerebral hemisphere opposite the side of the lesion is the first to suffer as it is being pressed against the unyielding cranial vault. With the variations in intracranial pressure (resulting from the organization of the blood-clot, or from the repeated venous bleeding

into the blood-cyst) which are sometimes initiated by dehydrating measures, there occur not only fluctuations in the state of consciousness, but also changes in the pyramidal tract signs.

Diagnosis.

The diagnosis of chronic subdural hæmatoma is not easy. Not infrequently there is the added difficulty of patients entering the hospital either in a state of coma, or so drowsy and stuporous as to make the history unobtainable or unreliable. In such cases a history of trauma may be sometimes obtained only after the operation when the patient has regained consciousness.

A history of mild trauma followed after a latent interval of several days, weeks or months, by headaches, vomiting and drowsiness should make one suspicious of a subdural hæmatoma. The latent interval may be of surprising duration, as for example the case reported by Buss [24] of bilateral subdural hæmatoma, which occurred three and one half years after the injury, and one and a half years after the onset of symptoms. That a patient may be able to carry on his usual occupation for a considerable period following his injury was observed in Case 2.

One of the most characteristic signs is the peculiar lethargic state of these patients, with alternating periods from stupor, drowsiness and coma, to consciousness within twenty-four hours or even less. Curiously enough the condition does not impress itself as being grave, and one hesitates to advise operation on so few signs. At times the patient appears as if he were naturally asleep or under the influence of a narcotic such as morphine. It is well to remember that this condition may readily be mistaken for acute encephalitis.

At times the diagnosis can only be made by exclusion and exploration. Chronic subdural hæmatoma should be seriously considered among the possibilities in the study of a patient in coma. Cerebral abscess and tumour may be most difficult to exclude. The alternating lethargic state is probably the most reliable finding in making the diagnosis. Studies of the spinal fluid and repeated observations of the fundi are often of little aid. The presence of a dilated pupil will invariably point to the affected side no matter what pyramidal tract disturbances may be present.

As a diagnostic procedure in difficult cases, trephining over the temporo-parietal region seems justifiable. The greenish-blue discoloration under the dura is unmistakable. One must not be misled by the absence of aphasia, for hæmatomas of surprising size covering

almost the entire left hemisphere have been found in right-handed individuals without the slightest evidence of speech disturbance during the lucid intervals.

Treatment.

Once the hæmatoma has formed it is most unlikely that spontaneous recovery will take place. Operation should be performed without delay.

This will vary with the condition of the patient. In instances where one has kept close watch of the variations in the size of the pupils, uninfluenced by homatropine or morphine, a trephine should be performed over the temporo-parietal region on the side showing a dilated pupil. The trephine can be so placed that if the patient's condition permits, one can proceed to do an osteoplastic craniotomy, or enlarge the trephine to approach a subtemporal decompression. With the aid of the sucker the entire clot and the greater part of the membrane can be removed through a subtemporal approach. Bilateral openings over the temporo-parietal region are advocated by most authors because of the high incidence of bilateral hæmatomata. There is also the danger that the removal of one hæmatoma will start up bleeding in the other.

It would seem wiser to inspect first the side that exhibits a unilateral dilatation of the pupil. If no evidence of a subdural hæmatoma is found, then the other side should be investigated, but in patients with no inequality of the pupils both sides should be inspected even if a hæmatoma has been found on one side. Bilateral operation is preferable to ventriculography because it is less upsetting to the patient and in instances where the hæmatoma is on both sides the ventricles are in the main collapsed and great difficulty is encountered. Ventriculograms under such circumstances are often unsatisfactory.

The clot should be removed completely and as much of the membrane as will come with it. It has been the consistent experience of those who have operated on these patients that subdural bleeding practically does not recur and that there is no fear in closing the wound without drainage. As might be expected, hypertonic solutions of glucose or saline given intravenously have been of little avail; on the contrary they seem to favour recurrent venous bleeding. As a general rule the patient regains consciousness shortly after the removal of the clot. Failure to react promptly means that the patient has either additional cerebral laceration or a hæmatoma on the other side.

The two post-operative complications to be feared in this condition

are cerebral œdema, which has been emphasized by Sachs [25], and extradural hæmorrhage which may follow any craniotomy, particularly when there is little or no increased intracranial tension at the time of operation.

Prognosis.

If in addition to a subdural hæmatoma there is cerebral laceration or subarachnoid hæmorrhage the outlook is very grave. The operation, if done early enough, will usually be followed by recovery. Of the forty-two cases referred to, 77 per cent. were operated upon and of these 83 per cent. recovered.

Summary and Conclusions.

(1) A study of eight cases of chronic subdural hæmatoma shows that this condition is frequently unrecognized despite the fact that it occurs more often than middle meningeal hæmorrhage.

(2) Experimental and clinical data show that trauma, often trivial, is the important ætiological factor.

(3) A rupture of an unsupported cerebral vein as it enters the superior longitudinal sinus will most often follow a blow over the occipital or frontal regions.

(4) The surprising latent period in the great number of cases can best be explained by slow and intermittent venous bleeding into the subdural space.

(5) The diagnosis of chronic subdural hæmatoma is based on a history of trauma, which, after a latent interval, is followed by the insidious onset of headache, drowsiness, vomiting and coma.

(6) The most characteristic clinical symptom of chronic subdural hæmatoma is a peculiar lethargic state which seems to alternate from drowsiness to coma, with periods of alertness and surprising response occurring within twenty-four hours or several days.

(7) Misleading pyramidal tract signs have been noted frequently in cases with chronic subdural hæmatoma. A dilated and fixed pupil on one side, even in the presence of a homolateral paresis or bleeding from the opposite ear, points to a lesion on the same side.

(8) In seven of the eight cases reported a unilateral lesion was present, and in one the hæmatoma was found on both sides. It is believed that in instances where there is a unilaterally dilated pupil, an opening should be made first on this side, but if inequality of the pupils

has not been observed a bilateral trephine should be done simultaneously even though a hæmatoma has been disclosed on one side.

(9) The term chronic subdural hæmatoma is preferable to pachymeningitis hæmorrhagica interna. The latter should be restricted to those instances in which the subdural bleeding has resulted from causes other than trauma.

I wish to take this opportunity of thanking Dr. Ernest Sachs and Dr. Foster Kennedy for their kindness and assistance in the study of these cases.

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LATERAL SYNDROME OF THE MEDULLA.

(Occlusion of the Posterior Inferior Cerebellar Artery. Vascular Lesions of the Hind-Brain).[1]

BY A. GREIG ANDERSON, R. D. LOCKHART, AND W. CLARK SOUTER.

The fertility of such cases of thrombosis of the posterior inferior cerebellar artery as a source of information regarding the retro-olivary region cannot be overestimated. As the anatomical, physiological and clinical significance of certain features is still unknown, this case is added to the literature in the hope that the variation of its details and the discussion of its problems may extend the knowledge, or at least indicate the obscurity, of certain aspects not dealt with in the publications consulted.

Similar cases were described by Senator [1], 1881, while the most recent accounts are by Thompson [2], 1929, Merritt and Findland [3], and Pines and Gilinsky [4], 1930. Good bibliographies may be consulted in the articles by Thompson [2], Merritt and Findland [3], and also in the work of Stopford [5].

J. T., a labouring man, aged 62, while at dinner on February 11, 1931, was seized with a sudden attack of giddiness and found he could no longer swallow.

He attended the Ear, Nose and Throat Department of the Royal Infirmary on the following day, walking half a mile to hospital, where he was seen by Dr. H. Peterkin, who reported as follows: "Much froth behind arytenoids and in piriform fossæ: an attempt to swallow resulted in laryngeal spasm."

He was admitted to the medical wards on the same day.

Clinical examination: The pupils are unequal, the left being much greater than the right. The left pupil reacts to light directly and consensually and on convergence. The right pupil reacts feebly to both light and convergence. The right palpebral fissure is narrower than the left. There is no diplopia or nystagmus. The ocular movements are full in all directions.

There is no subjective sensation of pain in the face. The sensibility of the corneæ to cotton wool is equal. The sensation of the face and auricle as tested to cotton wool and pin prick is equal on the two sides. Sensation of the tongue, gums, tonsils, palate and posterior wall of pharynx as tested to pin-prick is normal.

[1] From the Anatomy Department, University of Aberdeen.

The temporal and masseter muscles contract equally. The facial muscles contract equally on the two sides.

Hearing is equal on the two sides.

On phonation the palate moves upwards and to the left. The sterno-mastoids contract equally. The tongue is protruded straight. On subsequent examination this varied, the tongue being protruded a little to the right.

There is complete inability to swallow solids or fluids. There is frequent cough and expectoration of mucus. With attempts to swallow, the hyoid bone and thyroid cartilage move strongly, and no regurgitation occurs through the nose. The larynx is not affected.

There is no motor paralysis of the limbs or trunk.

FIG. 1.

The reflexes of the arms are feeble but equal on the two sides. The upper and lower abdominal reflexes are equal, but the cremaster responses are absent. The left knee-jerk is greater than the right, as is also the left ankle-jerk. The left plantar response is extensor, the right flexor.

Sensation in the upper limbs as tested to the usual modes, cotton wool, pin prick, heat and cold, vibration and passive movement, is normal. In the lower limbs light touch with cotton wool is appreciated equally on both sides. Pain sensibility is defective on the left limb and on the left side of the trunk up to the umbilicus. Heat and cold are not distinguished in this area. Vibration sensibility and the sense of passive movement are not impaired.

There is no disturbance of co-ordination. Gait and station are normal.

There is very little alteration in the tonus of his limbs; possibly it is a little increased in the left arm.

At subsequent examination the sense of taste, always a difficult and delicate problem, was found to be defective on the right side of the tongue, and one could pass the finger over the fauces and epiglottis without producing nausea. An opaque meal examination shows a complete hold up at the upper end of the œsophagus (fig. 1).

To Dr. W. Clark Souter we are indebted for the careful reports on the patient's eyes.

March 25, 1931. The right pupil measured 2·5 mm., the left 4 mm.

The right palpebral fissure is narrower. There is no enophthalmos. The right pupil acts feebly and equally to direct light and consensually; the left acts fairly well to light both ways. The right dilates not at all in the dark but the left dilates well in the dark. Both pupils act on convergence.

March 30: The effect of 3 per cent. cocaine hydrochloride on the eyes as regards size of pupils and height of palpebral fissure was estimated, a drop being applied to each eye at 9.45 a.m., and again at 10.45 a.m.

March 31: Ophthalmoscopic examination after homatropin and cocaine. Pupils dilated and circular, both optic discs have a whitish tint, with soft edges but without signs of previous neuritis; arteries of fair calibre with, here and there, a suggestion of some compression of the veins at the crossings, but no high degree of vascular degeneration.

On the right some superficial choroidal atrophy as an angular patch at the yellow spot area and to its nasal side, with three soft yellow spots at the outer side of that area.

On the left a sharply defined angular area of choroidal atrophy with three pigment dots just over the yellow spot area, and here some white tissue lies along the wall of a vessel that comes down from the superior temporal vessels, probably an artery which has thrombosed. The rest of the fundi seems normal.

It thus appears that in this case the right palpebral fissure and the right pupil were smaller than the left, but that under the stimulus of cocaine the right palpebral fissure opened up through 1·5 mm., whilst the left opened up through 2 mm., and further, that the right pupil opened up through 1·5 mm., whilst the left opened up 3·25 mm., the dilatation of the right pupil reaching its maximum in 2¾ hours, that of the left in 1½ hours. Practically no dilatation took place in the right pupil at 1½ hours, whereas the left had already begun to dilate at the end of the first 15 minutes (fig. 2).

The patient showed signs of cardiovascular degeneration with fibrillation of the heart. The Wassermann reaction of the blood-serum was negative.

The paralysis of deglutition persisted for some three weeks and then gradually subsided.

The patient was seen again some five months later, on July 27. He then stated that he felt perfectly well, and that he had no difficulty in swallowing, but that he had a curious sensation of warmth in the left leg from the knee downwards.

The pupils were still unequal, the left greater than the right, but the palpebral fissures appeared to be equal. The palate still moved up to the left. Taste was defective on the right side of the tongue. The nausea reflex had returned, i.e., stimulation of the pharynx with the finger now caused vomiting. The sensation of the left limb and trunk up to the umbilicus to pain and temperature was still defective. The left plantar response was extensor.

Dr. W. Clark Souter again examined the eyes with the following result:—

August 16: Now that the general clinical features had materially improved, a parallel series of observations was made to indicate the effect of cocaine on the palpebral fissure and pupil.

HOUR	PA. FISS. H.T.	P. SIZE.	R.	L.	P SIZE	PA. FISS. H.T.
	MM.	MM.			MM.	MM.
9·45	8·5	2.	•	•	2·5	11.
coc. 3% 10	9.	2·25	•	•	3·5	12.
10·15	9.	2·25	•	•	4.	12.
10·30	10.	2·25	•	•	4·5	12.
10·45	8·5	2·25	•	•	4.	11·5
coc. 3% 11·15	10.	2·25	•	•	5·5	13.
12·30		3·5	•	•	4·5	

FIG. 2.

HOUR	PA. FISS. H.T.	P SIZE	R.	L.	P SIZE.	PA. FISS. H.T.
	MM.	MM.			MM.	MM.
9·45	8.5	2·25	•	•	3·25	7·5.
coc. 3% 10	10.	3·25	•	•	4·5	10.
10·15	9.	3·75	•	•	5.	9.
10·30	9.	3·25	•	•	3·5	9.
10·45	10.	3·5	•	•	4.	9·5
coc. 3% 11·0	11.	3·25	•	•	3·5	10.
11·15	10.	3.25	•	•	3·5	10·5
11·30	10.	4.	•	•	6·25	10·5
11·45	11.	3·25	•	•	6.	12·5
12	10.	3·5	•	•	6·5	10·5
12·15	9·5	3·75	•	•	7.	8·5
1230	9	4·75	•	•	7·5	8·5

FIG. 3.

The general results show that the right palpebral fissure was slightly higher than the left at the commencement of the observations and reached its maximum of 11 mm. seventy-five minutes after the first drop of cocaine, whilst the left palpebral fissure reached its maximum of 12·5 mm. two hours after the first application, the fissures opening by 1·5 and 2·5 mm. respectively at the end of the first fifteen minutes. The right pupil was 2·25 mm. to start with and reached its maximum of 4·75 mm. nearly three hours after the first application of cocaine, whilst the left pupil, starting at 3·25 mm., reached its maximum of 7·5 mm. nearly three hours after the first drop. The increases in height of palpebral fissures and sizes of pupils are not steadily and evenly progressive, but the graphs of the pupil of this latter set of observations show much less disparity than those of the March observations. With regard to the palpebral fissure, the disparity between the two sets of measurements is rather less striking, as the accompanying diagrams show (figs. 2 and 3).

Discussion.

The inability to swallow even water, persisting for three weeks, is the salient feature of the case, and unique in the literature of the twenty-three cases consulted, where the dysphagia is confined to solids, though Foix, Hillemand, and Schalit [6] report a peculiar case which could swallow solids but not fluids.

The absence of the pharyngeal or nausea reflex may be the normal condition in some people, and we certainly found variation in this respect in our colleagues. In some normal people, as Pitres and Testut [7] express it, you may " promener " the finger around the epiglottis without result. The two most valuable signs of glossopharyngeal paralysis, according to Vernet [8], are the *mouvement de rideau* and the ability to swallow fluids but not solids. In our case, owing to paralysis of the right superior constrictor, stimulation of the left pharyngeal wall produced a drawn curtain movement towards the healthy side. Pitres and Testut [9] devote some fifteen pages to the discussion of the glossopharyngeal nerve. They regard it as supplying the superior constrictor, but Elliot Smith [10] declares that it supplies merely one muscle directly from the nucleus ambiguus, and that is the stylopharyngeus, which, according to the laryngologists [11] is of trivial importance in deglutition. In the main, leading authorities are agreed that the muscles of the palate and larynx are supplied eventually by the accessory part of the eleventh nerve. Divergence of opinion [12] in all probability is due not to defective observation but to slight variation in the pathways selected by the numerous axons of similar function from a composite nucleus in reaching their peripheral destination. For example, the sensory nucleus solitarius is responsible for taste, and no more divergent pathways from the tongue could be imagined than the routes of the chorda tympani and glossopharyngeal nerves. While the extremes of the minute solitarius mass may entrain with precision their definite routes, the fate of the individual nuclei from the intermediate zone must swing precariously in the delicate embryological balance for one road or the other when both are functionally identical, and this must be equally true when the motor nucleus ambiguus sends out its components via the ninth or the tenth or the eleventh nerves. In fact, the spinal accessory is a comparatively late comer in the phylogeny of the cranial nerves, for it is absent in fishes and amphibians, and first appears in reptiles, merely as an accessory root of the vagus. In the following it is not only simpler to concern ourselves with the nuclei of origin rather than with the nerves but more in accordance with our argument.

The symptom-complex of our patient is due to occlusion of the posterior inferior cellebellar artery, which, according to Stopford's [5] researches, supplies the dorso-lateral part of the medulla oblongata, although Foix, Hillemand and Schalit [6] maintain that in the upper part of the medulla this area is supplied by the artery of the lateral fossa, a branch from the basilar. They do not allude to Stopford's work, which is based on a larger number of cases. The degree of arterial variation, however, must always awaken reluctance to a rigid assertion regarding the implication of a particular vessel.

Damage of the spinothalamic tract accounts for the loss of pain and temperature on the opposite side of the body. We may deduce from this case that the fibres from the lower limb occupy the lateral portion of the tract.

Horner's syndrome is due to the affected pupillary nucleus which is placed by Combes [13] between the spinothalamic tract and the nucleus ambiguus, but Karplus and Kreidl [14, 15, 16] more recently maintain that the centre is in the hypothalamus (a point probably supported by the recovery of the pupil in this case), though they admit its mediation through the bulb. This medullary lesion does not produce such a marked contraction of the pupil as is seen in lesions of the sympathetic in the neck.

The nucleus ambiguus, partly affected, supplies the striated muscles of the palate, pharynx and larynx through the ninth, tenth, and eleventh nerves. Sachartschenko [17] states that 86 per cent. of cases of this type exhibit the triad of German authors, that is paralysis of palate, pharynx and larynx due to implication of the entire nucleus, but dissociation may occur, as in this case, the palate and pharynx together, or the larynx alone, being paralysed. Ramsbottom and Stopford [18] explain this as due to the rostral part of the nucleus ambiguus supplying the larynx, while the caudal part supplies the palate and pharynx; but Foix, Hillemand and Schalit [6], who investigated their case very thoroughly by serial section, came to exactly the opposite conclusion. From the embryological aspect it is more acceptable to regard the rostral part as innervating the palate and pharynx and the caudal part the larynx,[1] though the steps of development do not always conform to reasoned anticipation. The sensory nucleus solitarius, slightly affected, subserves taste through the ninth and tenth nerves and the pars intermedia of Wrisberg.

[1] Professor Stopford is in agreement with this criticism. (Private communication.)

The dorsal nucleus of the vagus escaped, but we believe that the spasm of the œsophageal entrance was due to irritation of this nucleus. Van Gehutchen and Molhant [19] say it supplies the striated muscle of the upper and middle parts of the œsophagus and the non-striated muscle of the intermediate and lower parts. This nucleus is considered also sensory by Elliot Smith [20], but Ranson [21] does not accord it mixed function.

Although the clinical diagnosis is certainly easy there remain difficulties of explanation, which were increased rather than diminished in the perusal of some thirty texts. Why could the patient not swallow fluids? According to Starling [22], in swallowing solids, elevation and dilatation of the pharynx is induced by the bolus initiating a sensori-motor reflex from the isthmus faucium, followed by constriction of the upper pharynx with dilatation of the lower in front of the advancing bolus, but in the deglutition of fluids a general dilatation secures their transmission almost at once to the stomach, hence the comparative immunity of the œsophagus in the swallowing of corrosive fluids. The hemiparetic pharynx may be unable to negotiate a rough bolus, but why should the healthy side not function enough to transmit at least a trickle of water? As a matter of fact, Spiller [23] argues that the subsequent ability of these patients to swallow solids is due to compensation by the healthy side. Mollison [24] states that complete unilateral paralysis of the tenth nerve has only a trifling interference with deglutition.

One possibility is that the dorsal vagal nucleus was impaired, with the result that the sympathetic exerted a tonic contraction. While this appears to solve the problem it is against the accepted teaching that stimulation of the vagus constricts the upper striated fibres of the œsophagus and dilates the lower non-striated fibres. Again the sympathetic influence is usually dilator. Such statements, however, are current among laryngologists. Brown Kelly [25] states that section of the vagi alone, without stimulation, gives dilatation of the œsophagus without relaxation of the cardia, which would be the final result if the innervation were purely vagal, but the supervening tonic contraction of the autonomous nervous system produces overaction or spasm. Kuntz [26] points out that section of the vagal fibres which supply the lower portion of the œsophagus and the cardia results in spastic contraction of these parts [36], the spasm subsiding after a few days, as the parts involved resume functional activity, which continues in an apparently normal manner. Brown Kelly further remarks that while dysphagia for solids is the principal symptom of œsophageal paralysis,

the dysphagia is rarely purely œsophageal and that motor and sensory paralysis of the pharynx are vitally important as affecting the second phase of deglutition. Then again Munro Cameron [27], after insisting that the inferior constrictor is continuous with the longitudinal fibres of the œsophagus, the striated muscle of which has no Auerbach's plexus between its layers, and that the "ascending pharyngeal branch" from the superior cervical ganglion supplies the inferior constrictor, leaves us to conjecture how far this sympathetic supply may determine the onset of spasmodic contraction, and continues that if sensation from the mucous membrane is abolished then the muscle does not react normally, and contraction is evoked by the presence of food on the muscle, or through some unusual sympathetic stimulation, with the result that spasm of this sphincter or any sphincter develops. Now Kuntz [28] mentions that no antagonistic action between the vagus and sympathetic innervation of the œsophagus has been shown in any animal; Samson Wright [29] states that there are apparently no sympathetic fibres to the œsophagus; Gaskell [30] considers there is no evidence that motor sympathetic fibres reach the œsophagus and that its motor supply is entirely vagal. Again, Hofer and Spiegel [31], having removed all possible source of œsophageal sympathetic supply, could find no alteration in deglutition, while Inoaka [32, 33] could elicit no reaction by stimulation of the extrinsic sympathetic nerves of the œsophagus in the dog. It is true that there are illustrations depicting a profuse leash of sympathetic fibres streaming to the œsophagus, but as careful dissection has not enabled us to find even a few, it is possible that these diagrams may have been reproduced from one text to the other without verification.

At the moment we would be inclined to submit the following explanations in this case.

(1) The lesion has just been sufficient to cause irritation of the dorsal vagal nucleus, with resulting spasm of the œsophageal entrance. In opposition to this view is the clinical argument against such an intensive spasm persisting for three weeks. The clinician might be inclined to suspect an upper motor neurone lesion, and this would be possible on the same side of the medulla because the fibres after crossing do not immediately reach their nucleus. On the other hand, the spasticity associated with an upper neurone lesion would take a few days to develop, whereas the spasm in our patient was evident at the onset.

(2) In view of the fact that our patient thought he was swallowing

when the food was really behind his cricoid cartilage, probably the sensori-motor reflex from this area was interrupted so that no inhibition was placed upon the dorsal nucleus to cause its relaxation. In fact Ranson [34] describes secondary fibres running from the sensory nucleus solitarius to the nucleus ambiguus and also to the dorsal nucleus, in explanation of the reflexes.

To both these views there is still the argument that the healthy side ought to function for the swallowing of water, but against that is the fact that the vagus is segmental in its distribution to the œsophagus, not one vagus to one side even in the upper part. This forces the conclusion that the right side of this patient's medulla is responsible for the upper spastic segment of his œsophagus.

Textbooks are vague or evasive on the subject of swallowing. Barclay [35] is of the opinion that we do not swallow at all, but suck. He insists upon the variations which occur in normal people, a probable explanation of clinical discrepancies. In the interpretation of such a case there are many difficulties due to our ignorance of the extent of striated muscle supplied by the nucleus ambiguus and the areas wherein these muscles are represented in the nucleus, and due to the fact that our knowledge of deglutition is both elementary and speculative.

Summary.

This article deals with a case of lateral syndrome of the medulla in a man of 62 years, exhibiting complete inability to swallow solids or fluids, Horner's syndrome of the right side, paralysis of the right side of the palate, defective sensation of taste on the right side of the tongue, abolition of the nausea reflex, *mouvement de rideau* of the pharyngeal wall, and defective sensibility to pain and temperature on the left lower extremity and trunk up to the umbilicus.

In the light of the conflicting views expressed in the literature, the anatomical, physiological, and clinical features of the case are presented with especial reference to the neurological mechanism of swallowing, and the condition of the pupils examined at the onset of the illness is contrasted with their subsequent examination, five months later, after partial recovery.

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A CONTRIBUTION TO THE CORTICAL REPRESENTATION OF VISION.

BY GORDON HOLMES.

THERE can be little doubt that the main lines of the cortical localization of visual perception in the area striata of the calcarine region of the occipital lobe as it is now generally accepted will ultimately prove correct. It is, for instance, definitely established that macular vision is represented near the pole of the hemisphere and the peripheral portions of the fields more anteriorly, while the upper quadrants of the retinæ correspond with the dorsal and the lower with the ventral parts of the areæ striatæ. It is generally accepted too that there is an accurate projection of the homonymous halves of the two retinæ on the opposite calcarine cortex.

Certain details of this localization still remain to be worked out. During the war of 1914-1918 I had the opportunity of examining several hundred men with gunshot wounds of the occipital lobes, and one striking observation which I made repeatedly during the early stages of such wounds was that, though the wound was apparently limited to one hemisphere, the blindness extended into the homonymous ipsilateral fields. In such cases the loss of vision almost invariably lay along the vertical axes through the fixation points, and generally became wider towards the upper or lower limits of the fields. I consequently called them "sector scotomata." This sector area of loss of vision might be found either above or below the fixation point, or both; it rarely extended to the upper or lower periphery. After observing a certain number of such cases it was found that such sector scotomata were generally caused by relatively large missiles of low velocity which had entered one occipital lobe obliquely or from the side and had been arrested by the falx separating the two occipital poles. I therefore concluded that the sector-like scotoma on the side of the wound was due to bruising or other damage of that portion of the calcarine area exposed on the mesial surface of the opposite hemisphere where this lies in contact with the falx.

This assumption was strengthened by a case in which a wound

immediately to the right of the middle line, slightly above the posterior end of the calcarine fissure, produced, in addition to left homonymous paracentral scotomata, right-sided sector scotomata extending from the fixation points downwards between the vertical meridians and the radii 20° from them ; it was found that two fragments of the skull had been driven through the falx immediately above the level of the posterior calcarine fissure in such a position that they probably injured only the upper superficial part of the left area striata.

From these and other observations I concluded that those portions of the retinæ which lie along the vertical meridians are represented on the exposed mesial surfaces of the occipital lobes, and, by exclusion, that the retinæ along the horizontal meridians are projected on to that part of the area striata which lies in the walls of the calcarine fissures [3, 4].

Later I discovered that Henschen [1, 2] had already suggested this further functional subdivision of the visual cortex. In a case in which Wilbrand had found by perimetric examination narrow homonymous scotomata extending from the fixation points along the horizontal radii to about 60°, Henschen demonstrated a small softening in the floor of the opposite calcarine fissure, and therefore concluded that the horizontal segments of the visual fields are represented in the bottom of the calcarine fissures.

The following case tends to confirm this conclusion :—

B. J., a married woman, aged 32, was admitted to the National Hospital on February 11, 1931, complaining of headache and disturbance of sight.

She came of a healthy family and her previous health had been good. Her first pregnancy terminated in a stillbirth, the second by Cæsarean section three and a half years previously.

For six months before admission she had suffered with headaches, chiefly on waking, and when the pain was severe she was conscious of a blowing sound in her head, mainly to the right side. In the middle of December, 1930, after an attack of influenza, the headaches became more intense in the temporal and occipital regions. A month later, during an attack of severe headache and vomiting, golden figures of simple types, as crosses, X's, and Z's, suddenly appeared in front of her eyes and her sight became dim. She was unable to remember if these figures and the dimness of vision were limited to any portion of the visual fields. This attack lasted about one hour but recurred next morning for a shorter time. Vision became normal quickly after each attack. Her headaches grew gradually more intense and were aggravated by sneezing, coughing or stooping.

On January 29, after a severer bout of headache her vision became again affected and, according to her own story, she lost consciousness for the next week. Her husband stated, however, that during this time she complained of

pain, replied to questions and took food, but lay immobile. Since this attack her sight has been affected, but it has improved a little; on attempting to read she has been unable to see words to the left of that at which she looked. Her limbs and speech have been unaffected, and she has not been subject to fits or convulsions. Her general health has remained good. Her cerebro-spinal fluid, obtained a few days after the attack of January 29, by her family doctor, was slightly blood-stained.

On examination she was a well nourished healthy looking woman. Her heart and blood-vessels were normal, and her blood-pressure within natural limits. There was a small port-wine-coloured nævus on her right cheek, lateral to the external angle of the orbit. She was bright and intelligent, and all her mental functions seemed to be normal.

Her ocular movements were unrestricted, but a slow coarse horizontal nystagmus developed on deviation to either side, consisting of slow recessions to the mid-line and quicker return jerks in the direction of voluntary deviation. The rate of the jerks was slower to the right. The left pupil was larger than the right, but both reacted to light and on convergence. The lower part of the left side of her face moved less briskly than the right on voluntary effort, but the functions of the other cranial nerves were normal. There was no disturbance of hearing.

The size and tone of her muscles were unaffected, but when unsupported her left arm did not maintain its posture as well as the right, and the left grasp was slightly weaker than the right. There was no disturbance of co-ordination. In walking she tended to deviate to the left and her left arm did not swing. Sensation was undisturbed. The left tendon-jerks were brisker than the right, but the abdominal reflexes were equal and the plantar reflexes were of the normal flexor type.

A month later she was slower in recognizing the shape of objects placed in her left hand than in her right, and on testing tactile discrimination with compass points she made mistakes on the left palm when the points were separated from one another to a distance at which she made no errors on the right palm.

She stated that on three occasions, at intervals of about half an hour on the one day, after someone had walked past the foot of her bed from left to right, she had for a moment or two the impression of the same person as before walking past, but when she looked carefully the person was not there. The dress, size and distance of the person appeared exactly the same, but the image was more shadowy.

Her visual acuity uncorrected was right $\frac{6}{12}$, left $\frac{6}{18}$. Her retinæ were normal, but the upper nasal quadrants of her discs were blurred, and later the upper edge of the right disc became œdematous. Her visual fields were repeatedly mapped out by different observers (fig. 1) and on each occasion a partial left homonymous hemianopia was found, the striking feature of which was that though the blindness came up to the fixation points along the horizontal meridians, there was a considerable escape along the vertical meridians in the

upper and lower quadrants. In the last fields which were charted (fig. 2), two days before her death, the blindness still reached the fixation point, but some recovery of vision was found, especially in the lower quadrants. The degree of hemianopia varied, probably under different functional conditions, as on one occasion (March 5) there was less escape in the upper and lower quadrants.

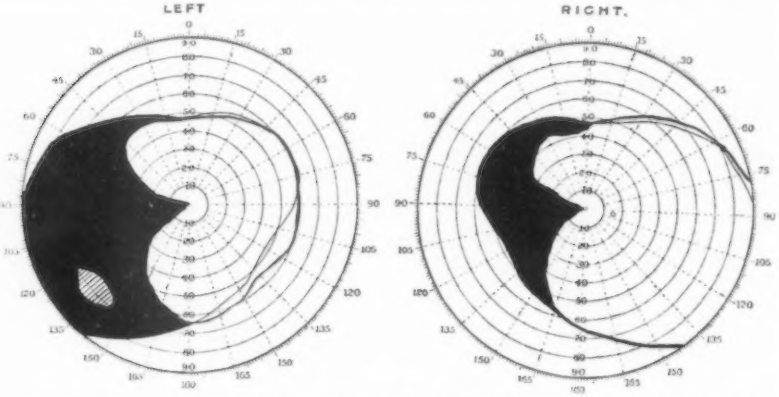

FIG. 1.—Visual fields recorded on February 20, 1931, with a white object one degree in diameter.

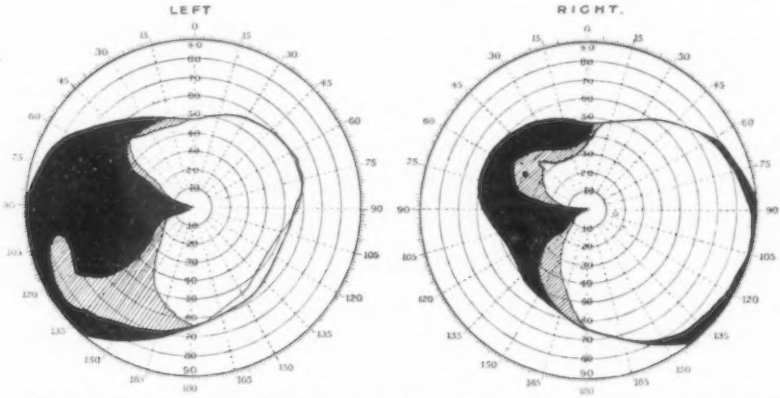

FIG. 2.—Visual fields on March 11, to a white object one degree in diameter. In the blackened area vision was completely lost, in the shaded areas moving objects were perceived.

Radiograms of the skull revealed no disease. On admission her cerebro-spinal fluid was clear and colourless, but it contained 15 small mononuclear cells per centimetre and the total protein amounted to 0·06 per cent. The Wassermann was negative in both the fluid and blood.

The diagnosis was made of a cerebral tumour in the right occipital lobe, probably involving the floor of the calcarine fissure.

On March 13, Sir Percy Sargent operated, opening the skull by a large osteoplastic flap over the right parieto-occipital region. The dura was under great tension, and before it was incised 20 c.c. of hypertonic saline was given intravenously to reduce pressure. On exposing the brain two enormously dilated vessels were found on the surface of the hemisphere, the most anterior being probably the Sylvian vein. They were connected by numerous anastomosing channels. A densely packed mass of vessels was also found on the lateral aspect of the occipital lobe. Owing to the severe degree of pressure and the patient's condition it was decided to make no attempt to deal with the condition at this operation. She died without apparent cause the same evening, forty-four days after the onset of the hemianopia.

Autopsy.—There was very little hæmorrhage at the site of operation. After removal of the brain a carmine gelatine preparation was injected under pressure into the right carotid artery after tying off the anterior communicating artery. The veins were also injected by a blue gelatine preparation.

On examining the brain several large vessels, some arteries, some veins, were seen to issue from the middle of the right Sylvian fissure. One large vein ran across the postcentral gyrus to the superior longitudinal sinus, another over the temporal lobe to the superior petrosal sinus. Other large veins connected with the lateral sinus and the posterior part of the longitudinal sinus. The arteries passed mainly backwards to a tangled, tightly packed mass of vessels, mainly injected red, on the lateral aspect of the occipital lobe in the position of the anterior occipital sulcus. The veins from this hæmangeioma drained into the longitudinal and lateral sinuses. The mesial surface of the hemisphere appeared normal.

After hardening in saline formaline the brain was divided by a series of coronal sections. In these it was seen that though the angeioma lay mainly on the surface of the brain many abnormally large vessels with thin poorly developed walls were present in the neighbouring and underlying sulci and a few penetrated into the white matter beneath the tumour. The cortex beneath and around the angeioma was damaged, probably at the operation or by the post-operative bulging of the brain into the trephine opening.

In addition a large hæmorrhage was found extending longitudinally through the occipital lobe, from the level of the hippocampus up to the tip of the pole. It was enclosed in an organized ochre-coloured capsule and in the hardened specimen seemed to be shrinking away from the capsule and the surrounding brain tissue, which seemed almost intact. It was evidently of considerable age, and its histological as well as its naked-eye appearance leave little doubt that its occurrence was responsible for the symptoms which appeared six weeks before death.

At its anterior end it lay lateral to and slightly below the wall of the posterior horn, but a little further posteriorly it broke into the ventricle and extended backwards in this position almost to the tip of the horn, to which it again lay lateral; behind the ventricle it occupied the white matter of the occipital lobe, directly opposite the bottom of the calcarine fissure.

The occipital lobe was cut in serial sections; every fifth was stained by the Weigert-Pal method and many intervening ones with carmine in order to study the structure of the tissues around the hæmorrhage. The most striking features of these sections was the clearly cut border of the lesion; the Weigert-Pal sections revealed very little injury of the fibres immediately around the hæmorrhage, and the changes visible in carmine preparations were slight. Within the hæmorrhage no nervous structures were visible.

One centimetre from the occipital pole of the hemisphere the hæmorrhage, which in its vertical diameter measured about 5 mm., lay in the white matter immediately lateral to the floor of the calcarine fissure, which was here represented by a shallow groove; all the tissues to within less than 1 mm. of the cortex were destroyed and the subcortical fibres rarefied (fig. 3). No changes were detected in the cortex. The upper and lower portions of the striate area and the white matter under them were unaffected. At this level the lesion extended lateral-wards to the cortex but did not involve it.

The hæmorrhage continued to occupy the same position in relation to the calcarine fissure as it was traced forwards to the annectant posterior cuneo-lingual gyrus where more subcortical white matter remained, but it was considerably rarefied (fig. 4). In front of this the lesion extended more dorsally, but the medullated fibres on the upper and lower walls of the fissure were well preserved and cortex was normal.

Where the ependymal cells of the posterior horn of the ventricle first appeared the coronal sections included the main mass of the angeioma. Here the hæmorrhage extended as a narrow horizontal slit, between $\frac{1}{2}$ and $\frac{3}{4}$ cm. in breadth, to the lateral aspect of the hemisphere, reaching but not involving the cortex. Its medial end came up to the non-patent tip of the horn and involved part of the sagittal strata here; there was also a small area of degeneration along the mesial border of the ventricle, immediately opposite the calcarine fissure. The fibres on the ventral margin of the horn were, however, not affected and stained normally.

From the opening of the posterior horn almost to the level of the hippocampus the lesion had broken into the ventricle, so that only its ventral part was recognizable in the sections. Most of the white matter on the floor of the calcarine fissure had disappeared or was represented by a few poorly stained fibres only, but in many places the cortex had escaped and presented surprisingly little histological change apart from a rarefaction of its radial fibres immediately above the lesion. The fibres of the sagittal strata around the ventral margin of the horn were preserved and stained well; the dorsal margin of these strata also escaped direct damage, though the fibres of the internal stratum at least did not stain as darkly as normally. The cortex along the walls of the calcarine fissure and that on the mesial surface of the hemisphere and the subjacent white matter were intact (fig. 5).

Towards the anterior end of the calcarine fissure, where the area striata is limited to its lower wall, the bottom of the sulcus was denuded of white matter and the middle portions of the sagittal strata were entirely destroyed, but the

FIG. 3.

FIG. 4.

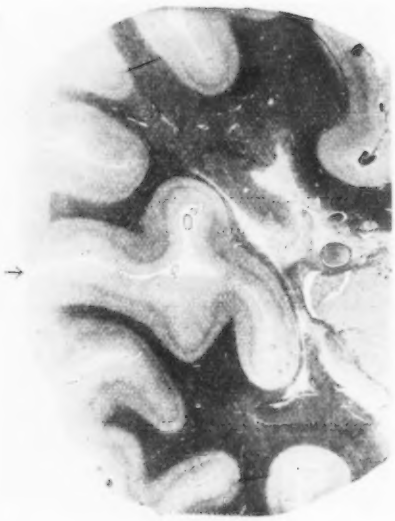

FIG. 5.

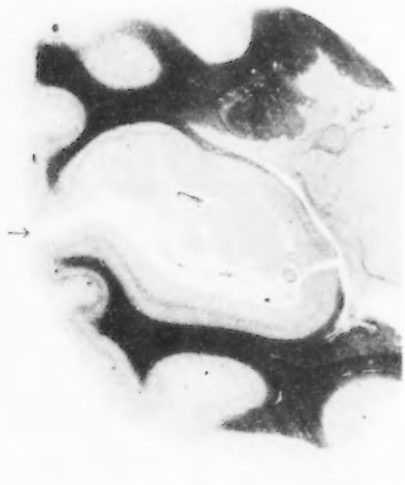

FIG. 6.

FIGS. 3-6.—Photographs of sections through the right occipital lobe stained by the Weigert-Pal method. In each photograph the calcarine fissure is indicated by an arrow.

dorsal and ventral margins of the strata were well preserved and fibres from them could be followed mesialwards into the white matter on the mesial aspect of the hemisphere (fig. 6).

Anterior to this level the lesion diminished in size, lay lateral to but involved the middle portion of the lateral wall of the posterior horn and extended through the middle part of the sagittal strata, but it left intact considerable portions of their dorsal and ventral margins.

One fact brought out by the histological examination of this case is the destruction of the middle portions of the sagittal strata of the occipital lobe by the hæmorrhage and the intactness of their dorsal and ventral fibres. In the Weigert-Pal preparations these stained quite well, and as the patient lived for forty-four days after the onset of the lesion sufficient time had elapsed for degeneration to have appeared in them if they had been interrupted in any part of their course. It is now generally agreed that the geniculo-calcarine fibres run mainly at least in the external stratum, that is the so-called inferior longitudinal bundle, rather than in Gratiolet's optic radiations, and it was in it that most fibres were preserved.

Further, the subcortical white matter along the floor of the calcarine fissure was involved along the whole length of the fissure to such a degree that few afferent fibres could have reached the cortex, and in places the cortex itself had suffered.

On the other hand the cortex and the subcortical white matter on the mesial surface of the brain and along the lips and the adjoining portions of the walls of the calcarine fissure had escaped injury and presented no evidence of disease or degeneration. Further, fibres could be traced from the dorsal and ventral borders of the sagittal strata into the white matter of these portions of the cortex.

From the site of the lesion and the structures involved by it, it seems justifiable to conclude that no afferent impulses could have reached those portions of the striate cortex buried deeply in the calcarine fissure and that therefore vision subserved by these parts of the cortex was lost, while the cortex on the mesial surface of the brain and along the lips of the calcarine fissure being intact and receiving afferent geniculo-cortical fibres was capable of function.

On correlating the anatomical lesions with the changes present in the visual fields it becomes probable that the sectors on each side of the horizontal meridians are represented in the cortex buried within the calcarine fissure, while the sectors adjacent to the vertical radii correspond with the striate cortex exposed on the surface of the

hemisphere and along the lips of the fissure. The greater loss in the peripheral portions of the homonymous fields, and the narrower area of blindness in the regions of the fixation points, would correspond with the larger proportion of the area striata affected or deprived of afferent fibres in the anterior calcarine region and the relatively smaller extent of the lesion towards the pole of the hemisphere (compare figs. 3 and 6).

This localization could be conclusively demonstrated only if the cortex alone was damaged, as it was in Henschen and Wilbrand's case, though here the lesion was too small to permit a general conclusion. In my case the middle portions of the sagittal strata containing the optic radiations were destroyed in a considerable portion of their extent. It is therefore necessary to assume that the dorsal and ventral fibres of the radiations carry impulses from the corresponding quadrants of the retinæ and pass to the upper and lower margins of the area striata. Henschen and others have postulated this anatomical arrangement, but unaware of his work owing to literature not being available to me during the war, I put forward the same conclusion from observations on gunshot wounds of the occipital lobes, and suggested that in the radiations the fibres are arranged regularly in laminæ according to the origin of the impulses they carry, and that those indirectly connected with the upper and lower quadrants of the retinæ are probably contained in distinct bundles separated by an anatomical interval [3]. Rönne [5] has come to the same conclusion. If this assumption is correct it would appear that impulses from the corresponding parts of the two retinæ are carried mainly in the fibres, uninjured in my case, on the upper and lower margins of the sagittal strata. Some of these fibres pass normally to the cortex in the depth of the calcarine fissure, but these must have been interrupted in the subcortical white matter by the lesion which involved this. The fibres to the upper and lower margins of the area striata were unaffected by this lesion and consequently able to reach the cortex on the surface of the brain and along the lips of the calcarine fissure.

It is probable that that portion of the lesion adjacent to the bottom of the calcarine fissure was the chief factor in determining the changes in the visual fields present in my patient, and the case is therefore further evidence that the sectors of the retinæ along their horizontal axes are represented in the cortex around the floor of the calcarine fissure.

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REFLEX-GRASPING ASSOCIATED WITH TUMOURS NOT INVOLVING THE FRONTAL LOBES.[1]

BY PAUL C. BUCY.

In neurology we are not infrequently confronted with a new sign or symptom which is advanced by its recorders as indicative of a certain pathological lesion. When the constancy of such signs can be adequately confirmed by numerous well-studied cases they become valuable aids to diagnosis; but when they are inadequately established they may be sources of error, especially in the localization of tumours, until their full significance is revealed.

In the past few years, reflex-grasping ("forced grasping"; "Zwangsgreifen," &c.) has received much consideration (Schuster [8 and 9], Schuster and Pineas [10], Schuster and Casper [11], Adie and Critchley [1], Freeman and Crosby [3], Janischewsky [5], &c.). It had previously been the subject of discussion by Janischewsky [4], Wilson and Walshe [12], and others. As a result, reflex-grasping has become associated by many clinicians exclusively with lesions of the frontal lobes. Adie and Critchley have gone so far as to say "that their presence (forced grasping and groping) in a patient with cerebral tumour is unequivocal evidence of the situation of the tumour (frontal lobe)."

Other authors have realized that such an extreme statement is not warranted. Janischewsky [5] states, "Die Bedeutung des Greifreflexes als fokales Symptom wird vermindert in den Fällen in denen ein Hydrocephalus internus vorhanden ist." Fedorovoa [2] has expressed a similar opinion, while Freeman and Crosby, speaking of the reflex in unconscious patients with generalized cerebral disease (not tumour), state, "It is bilateral and it does not have any especial localizing value."

I wish to describe two cases of tumour of the brain, one a tumour of the fourth ventricle with a marked internal hydrocephalus and the other a large neoplasm in the right occipital lobe, in both of which *bilateral reflex-grasping* was present.

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Case 1.—Convulsions, weakness, vomiting, headache, blurring of vision; stuporous and catatonic. Bilateral reflex-grasping, perseveration of movement, varied pyramidal signs. Ventriculography revealed right occipital tumour. Partial extirpation of a glioblastoma multiforme. Death six months later.

L. S., a male, aged 48, a Jewish shoe repairman, was referred to this clinic by Drs. Andrew Rosenberger and S. M. Turkeltaub of Milwaukee, Wisconsin. He was admitted on February 16, 1930, complaining of weakness and convulsions since September, 1929.

In September, 1929, while at work the patient was suddenly seized with a convulsion. He was told that he frothed at the mouth and "shook all over." He became unconscious and was taken to a hospital where he awoke several hours later with a cutaneous wound in the left temporal region. He returned to work the next day, although he complained of general weakness for several days. On the morning of October 27 at 2 a.m., the patient arose from his bed, vomited, cried out, and suddenly lost consciousness. In the course of a few minutes he had five or six generalized convulsive seizures, following which he was stuporous for the next twenty-four hours. During this time he was unable to say more than a few words because his tongue seemed thick and swollen; within four or five days his speech became normal. Three days after these nocturnal convulsions he returned to work, although he remained weak for several days.

On November 11, 1929, he was admitted to another clinic where examination revealed a depressed man, weighing 109 lbs. (he had lost 13 lbs. in the preceding eight weeks), with a blood-pressure of 115 84, and a pulse of 70. His vision was $\frac{2}{6}$ in the right eye and $\frac{6}{15}$ in the left. His visual fields on rough testing were not defective. There were no other abnormal findings. X-ray of the skull, examination of his urine and the Wassermann test on the blood revealed nothing abnormal.

He was discharged from the first clinic, in which the possibility of a brain tumour had been realized, on November 20, and was requested to return in a few months, but did not do so. Subsequently he had no more convulsions but became progressively weaker and gave up work about February 1, 1930.

Two weeks prior to admission to the Billings' Memorial Hospital of the University of Chicago, he had an attack of projectile vomiting, the first since the series of convulsions in October. On the morning of admission he vomited again. For about a month prior to admission he had suffered from headache over his eyes. For two months he had complained of blurring of his vision.

Past history: Seven years prior to the onset of the present illness the patient had fallen 25 ft. from a ladder, injuring his right shoulder. Ever since that time he has complained of pain in that shoulder and weakness of the right upper extremity.

These facts were elicited from the patient's relatives and the records of the other clinic, as he was too stuporous and un-cooperative to give a satisfactory story.

Examination (February 17, 1930): The left pupil was slightly larger than the

right; both were round and reacted sluggishly to light and more markedly so to accommodation. On ophthalmological examination of the fundi, marked blurring of the disc margins and a papillœdema of the two dioptres were seen. There were numerous hæmorrhages about the discs. It was impossible to determine the visual fields because of lack of co-operation.

A slight bilateral weakness of the external recti was present. There was a slight paresis of the left side of the face in voluntary movements; a definite weakness of the flexors of the head on the neck, with apparent atrophy of the anterior neck-muscles; some weakness of the extensors of the right forearm as compared to the left; a marked weakness of both deltoids; definite lateral displacement of the right scapula on extension of the arms, with atrophy of the muscles of the right shoulder-girdle. There was a tendency toward catatonia, the upper extremities remaining for considerable periods of time in any position in which they were placed. There was also a moderate increase in muscular rigidity which was of a plastic type, not unlike the "lead-pipe rigidity" of catatonic states.

There was a definite and obvious reflex-grasping in both hands. Whenever an object was drawn across the palms of the patient's hands the fingers closed upon it and grasped it firmly. Efforts to withdraw the object caused the force of the grasping to increase. The patient also experienced great difficulty in relaxing either the reflex-grasping or voluntary grasping.

There was also marked perseveration of movement, i.e., after a given movement was performed the patient persisted in repeating this movement several times. Strength was good in both lower extremities and no abnormality of movement was detected. The deep reflexes in the upper extremities were diminished but equal. The abdominal reflexes were active and equal. The patellar tendon reflexes were active and equal on the two sides, while the right Achilles-tendon reflex was more active than the left. The plantar reflexes were normal. The patient walked with short slow steps and occasionally tended to sway backward.

On February 18 conjugate movement of the eyes to the right was defective and there was a tendency to jerk back to the mid-line. The left wrist-jerk was brisker than the right and the left patellar tendon reflex was more active than the right. On this date the patient's slowness in comprehension was even more marked. He had difficulty in retaining ideas, in executing commands and on one occasion was unable to find his bed.

Because of the resemblance of this patient's condition to the catatonic states and because of the reflex-grasping it was thought that probably he was suffering from a tumour of one of the frontal lobes. However, as the lateralizing signs had not been consistent and because of the previous injury to the right upper extremity which made proper evaluation of signs in the upper extremities impossible, it was decided to resort to ventriculography in order to determine which frontal lobe was involved.

Ventriculography: On February 20, 1930, under novocain-anæsthesia, an incision and trephine opening were made in the right occipital region. A

needle was then inserted into the cerebral tissue and at a depth of 3 cm. entered a cystic cavity from which 5 to 6 c.c. of yellow fluid, which coagulated on standing, were obtained. It was obvious, therefore, that we had punctured a gliomatous cyst. The cystic cavity was filled with air and the wound closed. A similar opening was then made in the left occipital region. Clear colourless fluid was obtained from the left lateral ventricle and a small quantity (10 c.c.) of air injected. X-rays of the skull following this procedure revealed a small cystic space 2 to 3 cm. anterior to the occipital portion of the skull and 3 or 4 cm. above the level of the tentorium cerebelli.

Following the puncture of the cyst and the ventricle the patient was considerably brighter. Unfortunately the presence or absence of reflex-grasping was not recorded.

Operation: On March 1, 1931, an osteoplastic flap was reflected in the right parieto-occipital region. The cyst was again punctured and 10 c.c. of yellowish fluid were obtained. On reflecting the dura a greyish neoplasm was seen on the surface of the occipital lobe, about 4 cm. in diameter. As much as possible of the tumour was removed with the electric cautery, but as it was large and infiltrated the surrounding brain tissue, it was impossible to remove all of it. A decompression was made over the tumour and the wound closed.

Microscopical description (N-30-22): The tissue removed at operation was cellular. The nuclei varied greatly in size and shape and there were numerous mitotic figures. There was a goodly number of unipolar and bipolar spongioblasts present. Many multinucleated giant cells were seen scattered throughout the tissue. Cajal's gold-sublimate method revealed many spongioblasts, astroblasts and astrocytes. In some areas there was considerable extravasation of blood into the neoplasm and numerous small necrotic areas were seen. Intervascular necrosis, forming pseudo-palisades, was common. Throughout the neoplasm blood-vessels were very numerous. In some parts of their walls both the endothelium and the connective tissue showed considerable proliferation, which was well shown in preparation impregnated by Perdrau's method.

This tumour was a typical glioblastoma multiforme.

Course: Following the operation the patient had a rather stormy course partially due to the breaking down of the wound which drained for a long time following the operation. On one occasion a rubber tube which was being inserted into the cavity of the tumour was pushed into the lateral ventricle, resulting in a drainage of cerebrospinal fluid for two or three days.

He gradually recovered his general strength although he had a mild left hemiplegia. *Reflex-grasping was never elicited after the operation.*

On April 23, the visual fields showed a complete left homonymous hemianopsia with sparing of macular vision. Ophthalmoscopic examination revealed a mild secondary optic atrophy on the right.

The patient was given a course of Roentgen-therapy and discharged on May 11, much improved except for a small mass at the site of the decompression.

He was readmitted on May 28, because of continued growth of the mass

and slight breaking down of the wound. The mass continued to grow rapidly and he gradually developed a complete left hemiplegia. His general condition gradually became worse and he died on August 30, 1931.

Necropsy: A necropsy was performed fifty minutes after death. The findings, other than those in the nervous system, were moderate emaciation; acute hypostatic hyperæmia, œdema and broncho-pneumonia of both lungs; acute purulent bronchitis; brown atrophy of the myocardium and liver; atrophy of the spleen; moderate generalized arteriosclerosis; bilateral fibrous and calcified apical tuberculosis of both lungs.

Gross description of the cranium and its contents.—As the scalp was removed the tumour was found underneath it extending to the right mastoid, to the forehead and past the mid-line over the vault of the skull. The extra-

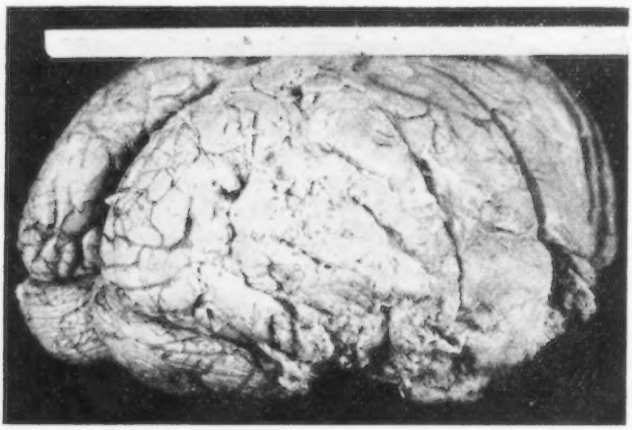

FIG. 1 (*Case* 1).—Glioblastoma multiforme occupying the right occipital lobe and extending forward into the temporal lobe. It also involves a small portion of the postero-inferior part of the parietal lobe.

cranial portion of the neoplasm was vascular and contained many small hæmorrhages. It measured 11 cm. above the surface of the skull and is 9·5 by 12 cm. in cross section. This was surrounded by a tough, white, avascular cartilaginous-like tissue. At the point of connection of the extracranial with the intracranial portion, the tumour was softer and contained areas of necrosis.

The intracranial portion of the tumour occupied the antero-inferior part of the right occipital lobe, the posterior portion of the temporal lobe and a small part of the postero-inferior area of the parietal lobe (fig. 1). The right hemisphere was larger than the left and there was a displacement of the median longitudinal fissure and the ventricular system to the left. There was no tumour in the anterior end of the temporal lobe, the anterior or superior portion of the parietal lobe or in the frontal lobes. Sagittal sections revealed the

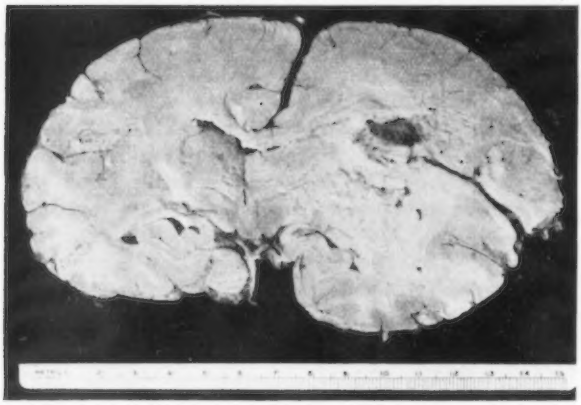

FIG. 2 (*Case* 1).—Anterior end of tumour lying lateral to the right thalamus in the region of the internal capsule. There is also a round mass of tumour lying in the Sylvian fissure. It is the same colour as the neighbouring cerebral tissue. This section is on a level with the anterior limit of the pons, a small portion of which is visible in this photograph.

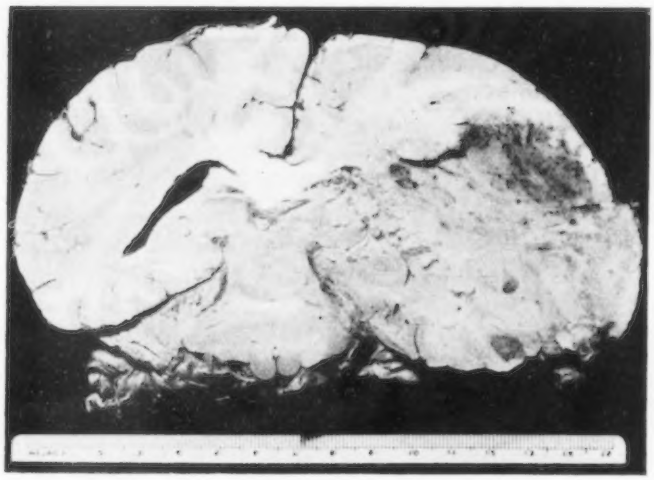

FIG. 3 (*Case* 1).—Coronal section through the centre of the neoplasm. There are numerous areas of hæmorrhage and necrosis.

anterior end of the tumour on a level with the anterior end of the pons. At this point it involved the internal capsule and extended medially to the lateral margin of the thalamus (fig. 2). It extended backward and downward from this point into the occipital and temporal lobes. The tumour was not encapsulated, was vascular and contained areas of hæmorrhage and necrosis (fig. 3). The lining of the lateral ventricles was ragged throughout.

Microscopical description.—The intracranial portion differed from the tissue removed at operation only in that there were numerous large areas of necrosis and hæmorrhage and an extensive ingrowth of connective tissue into some parts of the tumour.

The extracranial portion was composed of a dense connective tissue framework which enclosed small islands of tumour tissue similar to that within the brain. There were also many very large areas of necrosis.

The ventricular wall showed an absence of the ependyma, except in a few small areas, and a necrosis of some of the subependymal tissue.

Discussion.

It must be remembered that reflex-grasping was only observed in this patient in February 1931, prior to the operation. At this time the tumour seemed limited to the occipital lobe and posterior part of the parietal lobe. That portion of the tumour which at necropsy was seen to extend forward into the region of the internal capsule, the thalamus, and the occipito-frontal bundle is undoubtedly a late development which occurred during the six months that intervened between the operation and the patient's death. This is indicated by the absence of a hemiplegia prior to the operation. In any event a lesion in one hemisphere in this situation cannot be regarded as responsible for all reflex-grasping. Whatever the correct explanation of the presence of reflex-grasping may be in this case, it is obvious that it is associated with intracranial tension. There is no other apparent explanation for the fact that the phenomenon was present before operation and disappeared after a partial extirpation of the glioma had been done and a decompression made. Certainly the pathways involved in the production of the reflex-grasping could not have been destroyed by the neoplasm; more probably only a physiological block, which was removed with the relief of tension, was present.

The raggedness of the ventricular walls is in all probability secondary to the accidental puncture of the right lateral ventricle through an infected cavity and a resultant mild inflammatory process. It is also to be noted that at no time did this patient have a marked hydrocephalus.

Case 2.[1]*—Headache, vomiting, choked disc, paralysis of vertical conjugate movement of the eyes. Bilateral reflex-grasping. No operation. Death. Necropsy. Ependymoma of the fourth ventricle.*

This patient, a young girl between the ages of 15 and 20, was seen in the clinic of Professor O. Foerster, of Breslau, Germany. She presented the signs and symptoms of a markedly increased intracranial tension (headache, vomiting, choked disc, &c.). Clinically very few focal signs could be elicited except for a paralysis of upward movement of the eyes and a marked bilateral reflex-grasping—whenever her hand caught on the bedclothing, or when an object (such as the handle of a reflex-hammer or the examiner's fingers) was drawn across her palms, the fingers would immediately close firmly on the object and any effort to withdraw the object would cause the grasp to tighten.

The patient's condition rapidly became worse and she died before an operation could be performed. Necropsy revealed a severe internal hydrocephalus including a marked dilatation of the fourth ventricle upward. The ventricular system was obstructed by a relatively small tumour which proved to be an ependymoma in the posterior portion of the fourth ventricle. Except for the hydrocephalus there was no involvement of the cerebral hemispheres.

Discussion.

Janischewsky [5] has reported a case (No. 6) of cysticercosis of the brain, particularly of the base and of the brain-stem, with marked internal hydrocephalus, which presented bilateral reflex-grasping. Fedorovoa has reported one case (Case No. 5) in which a glioma of the right parietal lobe produced a complete left hemiplegia and marked reflex-grasping of the right hand. In another case (Case No. 6) reported by the same author, the patient presented the signs of increased intracranial tension and reflex-grasping of the right hand. A diagnosis of a tumour of the left frontal region was made, and it was decided to perform an operation. Just prior to the operation a weak reflex-grasping developed on the left side. The operation was performed, revealing a marked increased intracranial tension, but no tumour. At the time of the report the site of the tumour had not been determined. It is true that reflex-grasping has occurred in several cases of cerebral arteriosclerosis with dilatation of the lateral ventricles and atrophy of the frontal lobes (Freeman and Crosby, Cases 3 and 4; Schuster and Casper, Cases 16 and 17; Kleist [6] Case 10), but as the pathological lesion was one of atrophy rather than of internal hydrocephalus from obstruction

[1] Professor Otfrid Foerster, of Breslau, Germany, has very kindly permitted me to mention this case here. Because of other interesting findings he proposes to report it in more detail at a later date.

of the pathway of the cerebro-spinal fluid with resultant increased intra-ventricular tension, they do not seem to belong in this group. There was also evidence of atrophy of the frontal lobes in these cases of cerebral arteriosclerosis, while in the two cases reported here and in Janischewsky's case, No. 6, there was no evidence of any abnormality in the frontal lobes.

Several hypotheses have been advanced in explanation of reflex-grasping. It is not my purpose here to discuss all of these hypotheses or to offer one of my own. The hypothesis and schema of Schuster and Casper seem to be the most applicable to the largest number of cases, and possibly these cases may be interpreted in the light of their work.

Many authors have dwelt on the relationship of pathological reflex-grasping to the reflex-grasping seen in infancy. It is reasonable to suppose that the disappearance of reflex-grasping in the infant is due to the development and myelination of a transcortical inhibitory pathway to the pre-Rolandic motor area which suppresses reflex-grasping in the normal human subject after infancy, and that the development of pathological reflex-grasping results from interruption of this inhibitory pathway, or, as Schuster and Casper expressed it, deinhibition ("Enthemmung"). On this basis they have postulated the existence of a hypothetical inhibitory tract, which agrees with the known course of transcortical fibre tracts within the cerebral hemispheres and can be correlated with their pathological studies.

The hypothetical inhibitory pathway is bilateral in its origin, i.e., the inhibitory innervation of each central area arises in both frontal lobes. This inhibitory pathway arises from the medial surface of the superior frontal convolution and of the gyrus cinguli, and passes downward to the region of the occipito-frontal fasciculus which lies just beneath the corpus callosum, lateral to the lateral ventricle, and above the caudate nucleus, and inferiorly rests upon the internal capsule from which it is not sharply demarcated. These fibres then pass backward to the level of the central area where some pass directly to the pre-Rolandic area of the homolateral hemisphere, while others cross in the corpus callosum to terminate in the central area of the opposite side. The course of this pathway will be most clearly shown by the accompanying illustration from the work of Schuster and Casper (fig. 4).

It is extremely questionable whether the two cases reported here, Janischewsky's Case No. 6, and Fedorovoa's Case No. 5, can be brought

into accord with the hypothesis of Schuster and Casper. It is, of course, possible that the extreme degree of internal hydrocephalus in our Case 2 and the case of Janischewsky caused compression by the superolateral angle of the lateral ventricles in the region of the occipito-frontal fasiculus and thus of the "inhibitory pathway." Further, we might include Case 1 and Fedorovoa's Case No. 5 in which there was only a very mild dilatation of the ventricles (figs. 2 and 3) but a markedly increased intracranial tension, in such a hypothetical explanation. This appears to be a most fanciful explanation. However, as I have previously stated, it is not my purpose to furnish an explanation for this phenomenon, but I wish rather to stress the fact already established by

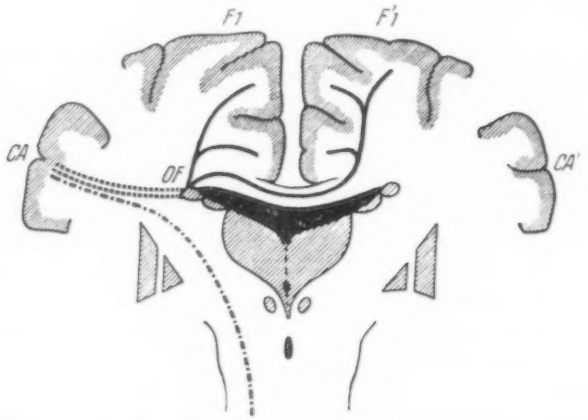

FIG. 4.—Schema of the "reflex-grasping inhibitory pathways." ——— and - - - - - the inhibitory pathway from the medial surface of the superior frontal convolutions (F1) and the gyri cinguli to the occipito-frontal bundle (OF) and thence to the central area (CA). ..... the pyramidal tract arising from the central or pre-Rolandic area (after Schuster and Casper).

Janischewsky and Fedorovoa that *in the presence of a marked internal hydrocephalus with increased intracranial pressure, the value of reflex-grasping as a localizing sign is greatly reduced.*

This is of little or no clinical value, for if we know the state of the ventricles in a given case of increased intracranial tension, a fact best established by ventriculography, we would also be aware of the presence or absence of a tumour in the frontal lobes. Therefore, it would be of much more value to establish some other criterion upon which we could judge the value of reflex-grasping in a given case. In the two cases reported here and in Janischewsky's Case No. 6 the reflex-grasping was

bilateral. As Freeman and Crosby pointed out, one cannot attach as much value as a localizing sign to bilateral reflex-grasping as can be attached to the existence of this sign on one side alone. This fact would seem to be of considerable importance in the evaluation of this sign. In thirty-five cases, including the two reported here (see Schuster and Casper and Fedorovoa), reflex-grasping was unilateral in twenty-six and bilateral in nine.

In those cases in which the phenomenon was unilateral, especially in the seventeen cases of neoplasm, the lesions are constantly located in the contra-lateral frontal lobe, with the possible exception of Fedorovoa's Case No. 6, in which the exact location of the tumour was not determined. Of those cases in which the sign was bilateral there are three, the cases reported here, Janischewsky's Case No. 6 and possibly Fedorovoa's Case No. 6, in which there was no involvement of the frontal lobes. In Fedorovoa's Case No. 5, there was reflex-grasping on the right side and a complete hemiplegia on the left. As reflex-grasping is known to disappear in the presence of a complete hemiplegia, it is possible that reflex-grasping may have been present on the left at one time. In two other instances, Cases 3 and 4 of Freeman and Crosby, the frontal lobes were involved in a generalized atrophy of the brain which was most marked in the frontal region. In Case 3 there were no focal lesions. In Case 4 there were two infarcts, one in the tissue underlying the left gyrus rectus and the other in the anterior limb of the internal capsule. In this case the white matter of the frontal lobes alone was atrophic. In the other three cases of bilateral reflex-grasping the lesions were in the frontal lobes. In Janischewsky's Case No. 2 the reflex-grasping was bilateral, more marked on the left side than the right, and autopsy revealed a large glioma involving both frontal lobes and the corpus callosum. In Freeman and Crosby's second case reflex-grasping was marked on the right side and slight on the left. Autopsy in this case revealed a tuberculoma on the medial surface of the left frontal lobe which compressed the corpus callosum and involved the right frontal lobe to a slight extent. Mayer's [7] Case No. 2 presented bilateral reflex-grasping, and at autopsy a glioma was found in the anterior part of the corpus callosum which extended into the white matter of both frontal lobes, the head of the caudate nuclei and on one side to the anterior portion of the putamen.

From these cases we may conclude that bilateral reflex-grasping may in some cases result from bilateral involvement of the frontal lobes, but in a large percentage of cases it was present in the absence of any

demonstrable lesion of the frontal lobes, or was associated with generalized and vague lesions. It is thus obvious that bilateral reflex-grasping is of no certain value as a localizing sign.

It might be well to state that it is not the purpose of this article to attempt to detract from the work of previous observers which seems to establish the value of this sign, when unilateral, in the localization of frontal lobe lesions. The number of cases in which this contention has been borne out is far too great. However, as in the case of all other clinical phenomena, a given sign is only of real value when we are aware of its indications in a given case and its limitations under known conditions.

Conclusions.

(1) Two cases of tumour of the brain in regions other than the frontal lobe in which marked bilateral reflex-grasping was present, are reported.

(2) Reflex-grasping in the presence of a marked internal hydrocephalus with increased intracranial tension is of little localizing value. This is particularly true when the sign is present bilaterally.

(3) Bilateral reflex-grasping is at all times of questionable value as a localizing sign.

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THE RATE OF CONDUCTION IN THE HUMAN MOTOR NERVE.

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THE velocity of conduction of impulses in human motor nerves has, in spite of numerous investigations, remained an unknown quantity up to the present. The comparative paucity of recent work, in the face of the unsatisfactory nature of all previous results, may possibly be due to a certain lack of interest in an apparently academic problem. This attitude seems to be fundamentally wrong. As the formulation of reflex mechanisms increases in precision, the time may well arrive when temporal measurements will afford a clue to the better understanding of the particular elements involved in a nervous reaction.

The figures for the velocity of nerve impulses available at present not only show a complete lack of agreement between the various observers, but in the hands of no single observer are the results consistent. This will clearly be seen from the following table of velocities in human motor nerves.

Observer	Mean velocity per second	Maximal value	Minimal value	Nerve	Site of stimulation
Helmholtz and Baxt (1867)	39·9 m.	37·5 m.	31·0 m.	Median	Wrist and upper arm
Kohlrausch (1866)	94 m.	—	—	—	—
Donders (1868)	26 m.	—	—	—	—
Helmholtz and Baxt (1870)	64·56 m.	89·4 m.	36·47 m.	Median	Sulcus bicip. internus and wrist
Place ..	35·25 m.	62 m.	17·24 m.	,,	Lower margin of deltoid and wrist
Ochl	Warming 50 m. Cooling 25 m. Normal 30 m.	78 m. 35 m.	36 m. 20 m.	—	—
Alcock ..	66·8 m.	—	—	—	—
Hermann ..	41·85 m.	—	—	—	—
Piper	120 m.	131-139 m.	107-113 m.	Median	Sulcus bicip. internus axilla
Münnich ..	66 m.	81 m.	55 m.	,,	,, ,,
Schäffer ..	64·3 m.	74 m.	54·4 m.	Sciatic	Electric stimulation deep reflexes
Felix ..	45·50 m.	63·4 m.	43·5 m.	,,	,, ,,

Previous to the experiments of Piper, all observers had depended on some form of mechanical registration of the muscle response, and their results had given figures which, however discordant *inter se*, agreed in assigning a velocity of less than 100 m. per second to the motor nerve. Piper, for the first time, obtained electromyographic records of the voluntary contraction of human muscle by means of the string galvanometer, and was then led to estimate the velocity of conduction in the median nerve by stimulating it with break induction shocks in the axilla and in the bicipital groove, the current produced by the muscular response being led off from the muscles of the forearm to an Einthoven galvanometer. The conduction times obtained were far from uniform, ranging between 107 and 139 m. per second. The mean velocity was estimated at 120 m. Dodge claims to have confirmed this result, without, however, publishing any figures; using a very rapid falling-plate camera, one of us has obtained values between 120 and 145 m. per second with the Piper method.

Munnich, using the same points of stimulation, adjusted the relative strengths of the two stimuli in such a way that the electromyograms obtained were exactly congruent when superimposed. His measurements also showed wide variations (81 to 55 m. per second), but gave a mean velocity of about half that claimed by Piper.

Schäffer stimulated the sciatic nerve in the popliteal space and at the level of the hip-joint, and obtained a mean velocity of 64 m. This is almost identical with Münnich's figure, with practically the same limits of variation (74 to 54·4 m. per second).

Hoffman observed that the stimulation of the motor nerve to a muscle (by a single induction shock) causes, in the intact animal, a secondary reflex electrical response to follow the original direct response. Felix made use of this observation, and recorded this reflex response in the short extensors of the toes, stimulating at the internal malleolus; in the calf muscles, stimulating in the popliteal space; and in the muscles of the forearm, stimulating the median at the elbow-joint. He calculated the velocity of the impulse from the length of nerve tract involved in the reflex arc, and found a mean velocity of 45 to 50 m. per second. Although his extreme figures are 63·4 and 43·5 m., the mean deviation is relatively smaller in his results than in those of other observers.

It is obvious that this wide divergence of measurements, from the values of Piper downwards, cannot be explained by the possibility of a functional variability alone. Münnich was the first to point out two

potential sources of error in Piper's method. The first lies in the assumption that an electrode, placed over a deeply-seated nerve, produces strictly local stimulation of that nerve. Such localization is only possible where the nerve is practically subcutaneous, and it was found experimentally that the area of spread of potential excitation is proportional to the amount of tissue intervening between electrode and nerve. Secondly, Piper was forced to use a far greater strength of current for the stimulation of the median nerve in the axilla, where it is deeply placed, than in the bicipital groove, where it is superficial. There was thus a second factor making for the spread of the area of excitation, quite apart from the fact that the electromyographic responses from the two points of stimulation were of different sizes.

It was by paying great attention to the latter point that Münnich claimed to have obtained results far more reliable than those of Piper. He discarded all records in which the two curves could not be accurately superimposed, so that his calculations were based on strictly comparable responses. In spite of this precaution, however, the above quoted figures of Münnich show too much divergence to be of value. That this divergence is inherent in his method and independent of the fallacy connected with the position of the nerve and the size of the muscular response is obvious from his experiments on the exposed motor nerves of animals where the proximal and distal stimuli were of the same strength. In these experiments, moreover, differences of temperature were also taken into account, but neither precaution led to a greater uniformity of results. The results are shown in the following table:—

Temperature	Animal	Length of nerve	Minimal value	Maximal value	Mean velocity per second
38·9° C.	Rabbit	61 mm.	59 m.	64 m.	61 m.
38°	Cat	73	67	82	75
38·2°	,,	80	81	82	81
38°	Dog	72·5	77	102	88
38°	,,	77	59	65	61
37·8°	,,	90	70	92	85

A reconsideration of the problem has revealed at least two other sources of error which were not excluded in the methods hitherto employed, and which may well be the cause of the lack of agreement among results in the past.

An inspection of the electromyograms published by Münnich shows that the exact point of inception of a curve cannot be determined with accuracy, but that they admit, at their best, of a possible deviation of 0·5 sigma in either direction. In some of the published records the

possible error is considerably greater. When dealing with short stretches of nerve, as in the animal experiments, an error of 0·5 sigma may double the estimated velocity; but even where greater lengths of nerve tract are involved—e.g., 19·5 cm. in man—the same error can shift the estimated velocity from 66 to 55 m. on the one hand, or to 78 m. on the other. The electromyograms of Schäffer and Felix, which were taken at a slower speed than Münnich's, show an even greater possible error, while Piper's original records were photographed at a very high speed and are relatively, though not wholly, free from it.

All previous observers have used the break induction shock for stimulation, and it is in this that the second source of error lies. Bernstein showed that the duration of a break induction shock may amount to 2 to 3 sigma. Thörner, using an inductorium with an iron core, in circuit with 2 cm. of nerve, gives the duration as three sigma.

The importance of this for the experiments under consideration was emphasized by Steinhausen, who pointed out that we have no means of telling at what point, in the course of the three sigma, the nerve impulse is actually transmitted; that is to say, what phase of the wave of potential represents the effective concentration of current for stimulation. Even in experiments on isolated nerves, where the two successive shocks are delivered with the coil distance unaltered, it must not be assumed that the effective concentration of current is reached at identical points on the two curves. If now we turn to the experiments on human subjects, where the nerve has to be stimulated successively in superficial and in deep positions, so that different intensities of current have to be employed, it is fairly certain that stimulation will occur at appreciably different points on the potential curves.

Concerning the method to be described, it is claimed that the sources of fallacy detailed above have been excluded, and the following requirements satisfied :—

The point of inception of the muscle response can be established within a limit of error not exceeding 0·08 sigma; this error is, for practical purposes, negligible.

The stretch of nerve between the two stimulated points can be measured within an experimental error of $\pm$ 2 per cent., a far smaller figure than could obtain in previous experiments.

The stimulating electrodes are not separated from the nerve by any tissue other than skin and a thin layer of superficial fascia.

The duration of the stimulating current is below 0·1 sigma.

Method.

The essential feature of the method is the use of a pendulum or spring contact breaker, by means of which a given circuit can be closed and broken again within an exceedingly brief interval. The second important feature is the substitution of a condenser discharge for the break induction shock in stimulation.

The contact breaker (spring type of Keith Lucas) has two keys; one fixed and one movable along a graduated arc. In the present experiments the first key was used for the administration of the stimulus (condenser discharge), while the second key was connected in series with the string galvanometer, by means of which the resultant muscle

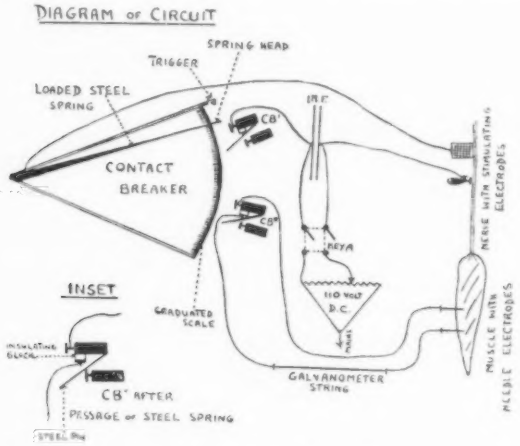

Fig. 1.—Diagram of circuit.

twitch was registered. Both keys are worked by the release of a loaded steel spring which swings horizontally over the graduated scale at a fixed rate; the time equivalent of one division on the scale is 0·175 sigma. Each key (model used by Keith Lucas with his pendulum) consists of a steel pin held in electrical contact with an adjustable knife edge by means of a small spring In the original design the swing of the loaded springhead knocked the steel pin from the knife edge into a neutral position, thus breaking the circuit. For the present experiments the first key had to be modified in such a way that electrical contact only existed momentarily while the springhead was passing over the steel pin. This was achieved by bringing the springhead, instead of the

knife edge, into circuit with the steel pin, electrical connection depending on the fact that the free end of the steel pin, by virtue of its elasticity, yields slightly to the impact of the springhead, and its contact with the knife edge is not broken until it has been in contact with the springhead for an instant. The second key was used as a contact breaker, the swing of the springhead throwing the galvanometer out of circuit. In this case it was necessary to slip an insulating sleeve over the projecting end of the steel pin, so as to avoid cross-connection with the stimulating circuit via the springhead. The galvanometer was a double string Cambridge model, but one string only was used in these experiments.

Procedure.

The Lucas keys CB′ and CB″ were set as shown. The source of current, a 1 MF condenser, was charged from the mains by momentarily closing key A. The loaded spring was then released by pulling back the trigger, and it knocked the keys CB′ and CB″ into the position shown in inset. The charging voltage could be varied by means of a rheostat, and was adjusted so that the condenser discharge produced a submaximal stimulus with an easily bearable sensory effect.

The nerve chosen for stimulation was the ulnar nerve, and the points stimulated were in the ulnar groove at the elbow-joint, and a point at the wrist where the nerve becomes superficial on displacement of the flexor carpi ulnaris tendon. In both positions the nerve is virtually subcutaneous, and the area of stimulation was restricted to a minimum by using a small button electrode which could be pressed well against the nerve. In each case the indifferent electrode consisted of a large padded zinc plate, bandaged over the upper arm. The electrodes were connected to key CB′ as shown in the diagram.

The recording electrodes were two fine steel needles, connected in series with the galvanometer and the second key (CB″); these were plunged into the substance of the abductor minimi digiti muscle, about 2 cm. apart, and placed in line with the long axis of the muscle. The proximal needle was about 4 cm. from the stimulated area at the wrist.

It will be evident from the connections of the recording circuit that the registration of a muscular response is only possible before the springhead has passed key CB″. If, therefore, CB″ be moved so close to CB′ (stimulus) that the galvanometer is thrown out of circuit before the response has occurred, there should be no galvanometer deflection

other than that due to the polarization current of the skin and the capacity effect of the subject's body. It was found that the capacity effect could be easily rendered negligible by providing a permanent leak with a resistance of 10,000 ohms between the needle electrodes. The polarization effect, with the type of needle used, was of a far smaller E.M.F. than the action current. It was therefore possible to adjust the galvanometer so that the polarization current caused no deflection at a sensitivity at which the current of action was still appreciable. During an experiment the presence or absence of a galvanometer deflection was observed directly. The stimulating electrode was first placed over the nerve in the ulnar groove and key CB″ moved up opposite CB′. In this position stimulation produced of course no galvanometer deflection. CB″ was then moved away from CB′ until a deflection in response to stimulation could just be observed. The point at which the galvanometer response occurred could be localized with great sharpness to within half a division on the scale, that is, to 0·08 sigma. In every instance the genuineness of such a positive result was verified by a blank experiment, in which the experimental conditions were identical except that the button electrode was not on the ulnar nerve, but at some neutral point on the forearm. A uniformly negative result in these circumstances was accepted as proof that the galvanometer excursion actually represented the contraction of the abductor minimi digiti muscle. All positions on the scale beyond that point obviously gave positive results. Let the point be known as position A.

In the second set of experiments the whole procedure was repeated, but with the button electrode at the wrist. In this case the distance between CB′ and CB″—when a galvanometric response was first obtained—was very short. This position of CB″ was denoted point B. The time equivalent of these two points then represents the time taken by the nerve impulse to travel from the stimulated area at the elbow to that at the wrist.

To determine the time taken by the springhead to pass from position A to position B, both keys were converted into contact makers and connected each with one string of the galvanometer and a millivolt charge circuit. The strings were so adjusted that closure of the circuit deflected each string sharply and through the same distance. Simultaneous photographs of the deflections due to successive making of the keys were taken during the swing of the springhead at fairly high speed. The velocity of conduction was calculated from the data thus obtained and from the length of nerve measured between the two stimulated points.

The velocity of motor nerve conduction was studied exhaustively in the subject G. The results are tabulated below:—

ULNAR NERVE.

Date	Latent period electrode at wrist	Latent period electrode at elbow	Nerve length	Mean velocity
13.7.31	6 sigma	8·8 sigma	31 cm.	37·8 m. per sec.
15.7.31	6	8·7-8·9	31	38·2-37·3
22.7.31	6	8·8	31	37·8

Needle electrodes in abductor minimi digiti muscle, 4 cm. from stimulating electrode at wrist.

Velocity of nerve impulse = 37·8 m. per second.

On each of the dates some twenty or more observations were made, and in each case, except in some of the readings of the 15th, no perceptible variations were noted. In other words, the efficiency of the method is such that no significant discrepancies of results are encountered. Were it possible to measure the length of nerve between the two points of stimulation with equal accuracy, the velocity of conduction could be determined within 1 per cent. of error. This is unfortunately not the case, the possible error in nerve measurement being + or − 1 cm.

In the above cited results a nerve length of 32, instead of 31 cm., would raise the velocity from 37·8 to 39·2 m. per second; and a nerve length of 30 cm. would bring it down to 36·5 m. per second.

This difficulty of accurate measurement should not be insuperable, given a sufficiently large number of observations on dissecting-room material from which the relationship between nerve length and length of ulna from olecranon to styloid process could be worked out with accuracy.

In a further attempt to settle this point a series of observations were made on the same subject using three points of stimulation of the ulnar nerve.

The distal point remained as before at the wrist; the middle point was just below the ulnar groove and 29 cm. from the wrist, while the proximal point was 2 cm. above the original site at the elbow, the electrode being pressed well on to the nerve, displacing the triceps tendon outwards; this point was exactly 35 cm. from the wrist electrode. The figure for the distal electrode still remained 6 sigma; for the middle electrode it became 8·2 sigma, and for the proximal electrode 9·5 sigma: the velocities for these two positions were 38·3 m. and 39·1 m. per second respectively. These results are in fair agreement with the original set of figures, when the fact is taken into consideration that the proximal stimulus—on account of the slightly deeper position of the nerve—is not strictly comparable with the others.

Three other subjects offered themselves for experiment and gave the following results :—

ULNAR NERVE.

Date	Subject	Latent period electrode at wrist	Latent period electrode at elbow	Nerve length	Mean velocity
23.7.31	T	6 sigma	9·2 sigma	31 cm.	36 m. per sec.
29.7.31	H	6	8	26	35·1
30.7.31	J	6	8·2	28	36·8

Needle electrodes in abductor minimi digiti muscle, 4 cm. from stimulating electrode at the wrist.

In each of these subjects repetition of the experiment gave identical readings on some twenty occasions. We regard the lack of uniformity of the results of these three subjects *inter se* and their divergence from the values obtained on subject G as being an expression of the difficulty of assessing with accuracy the length of nerve between the points stimulated.

In only one subject (G) was the median nerve used for a similar experiment, and in this case the needle electrodes were plunged into the small muscles of the thumb on the thenar eminence. This nerve was far less suitable than the ulnar, owing to its deeper situation. Again, the most superficial parts of it were chosen for stimulation, the distal point being at the wrist, where on lateral displacement of the flexor tendons the nerve could be pressed against the styloid process of the radius ; the proximal point where the nerve lies along the medial border of the biceps, the electrode being pressed outwards and under the edge of the muscle. The distance between these two points was 39·4 cm., and the distal electrode was 5 cm. from the needle electrodes. The figures obtained were 7 sigma for the distal point, and 11·4 sigma for the proximal point, giving a velocity of 36·8 m. per second.

In three subjects additional readings were taken for stimulation of the ulnar nerve in the axilla, and in one subject for stimulation of the median in the axilla. The results are given below :—

ULNAR NERVE.

Subject	Latent period electrode at wrist	Latent period electrode at axilla	Nerve length	Mean velocity
G	6 sigma	15·6 sigma	62 cm.	41 m. per sec.
G	6	15	62	43
T	6	14·7	60	43
J	6	13·7	56	42·7

MEDIAN NERVE.

G	7 sigma	13·6 sigma	56 cm.	43 m. per sec.

These readings were taken more for the sake of completeness than with a view to corroborating former results. They agree, *inter se*,

very closely, but cannot be accepted as valid, because of the greatly exaggerated possible error in nerve measurements. The nerve not only passes over two joints so that the estimates vary according to the position of the joints, but it is deeply seated in the axilla, thus affecting both the localization of stimulus and the accuracy of measurement. The results obtained from the ulnar nerve in the forearm are therefore held to be the nearest approach to a true value for the velocity of conduction of motor impulses.

Though these experiments afford no evidence that there is any appreciable difference in conduction rate between the upper and lower portions of a motor nerve, such as the ulnar, it was thought possible that the velocity of conduction in its terminal intramuscular branches might be reduced. In a study of the human deep reflexes by one of us in conjunction with Dr. Cook it was pointed out that, with direct electrical stimulation, the rate of propagation of a contraction along the rectus femoris muscle was 20 to 30 m. per second (stimulus = single induction shock). Owing to the obvious difficulty of accurately localizing the point of stimulation in this case, we decided to repeat the experiment on the same muscle, but with indirect stimulation—using the patellar reflex response. Before selecting two points on the muscle from which the electrical response was to be led off, it was necessary to determine the level of entry of the nerve, or the "nervous equator" of the muscle. Only then could one be sure of the direction of the response. The muscle was accordingly explored along its entire extent by two pairs of needle electrodes set 2 cm. apart, and moved successively from a proximal position near its origin, to within a short distance from the upper border of the patella. In a muscle measuring 43 cm. in length, the nervous equator was found to be represented by a transverse band, 3 cm. broad, lying about 14 cm. below the anterior superior spine. Above this band, the electrical response travels upwards; below it, it travels downwards. When one electrode is placed just above the band, and one just below it, the electromyogram presents a triphasic curve. Piper had already drawn attention to this triphasic response whenever the electrodes happen to be placed athwart the nervous equator. In a discussion of its significance, he offered what appears to be a convincing explanation of its origin, namely, that it represents the resultant of the ascending and descending action currents. In a criticism of the interpretation of similar triphasic curves, recorded by Golla and Cook, Pritchard casts doubt on Piper's view. Fig 2 is a reproduction of Piper's original diagram.

Fig. 3 shows the reversal of the direction of the electrical response above and below the nervous equator, and the triphasic response when the electrodes are placed athwart the narrow band of the nervous equator.

Having determined the position of the nervous equator, it became necessary to ascertain whether the contraction reached all points on any particular transverse level of the muscle simultaneously. This was done by leading off from two pairs of needle electrodes, each connected to one string of the galvanometer, and plunged into the muscle along a straight transverse line. The response was found to be simultaneous in the two pairs.

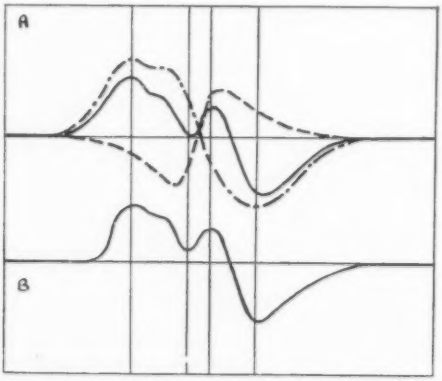

Fig. 2.—Diagram after Piper. In the group A, curve —.—.—. represents an actual electromyogram from above the nervous equator, and curve — — — an actual electromyogram from below the nervous equator. The unbroken line is the resultant of the two curves superimposed. B represents an actual electromyogram obtained from electrodes, one above, and one below the nervous equator. Note the very close correspondence between this curve and the above, arrived at by calculation.

Measurements of velocity in intramuscular nerve fibres could now be undertaken and were made in the manner just described, but with the two pairs of needle electrodes 12 cm. apart; both pairs, of course, were below the nervous equator, so that the response was unidirectional. The distance between the needles in each pair was about 0·5 cm. Fig. 4 shows the electromyogram of the patellar reflex thus recorded. The velocity of the descending response is 29 m. per second, or 10 metres slower than in the ulnar nerve. As some difficulty was experienced in obtaining good electromyographic records with strings loose enough to respond to such small currents, the experiments were repeated with the inclusion of two-valve amplifiers in the circuits, giving a tenfold

amplification of the muscle currents. The strings could now be kept at a fairly high tension, and gave sharp and accurately readable deflections. Measurements of these showed a velocity of 29 m. per second—that is, identically the result quoted above.

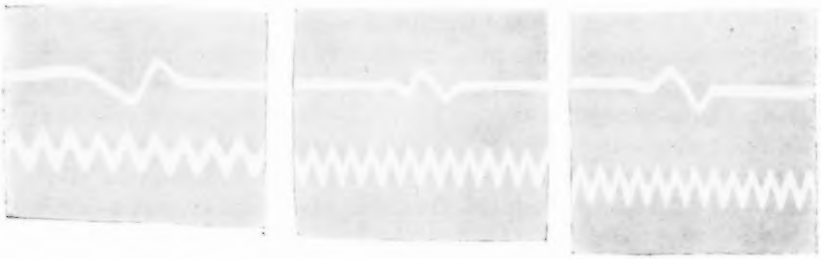

FIG. 3.—Electromyograms of rectus femoris from three positions. Left curve obtained with both electrodes above the nervous equator; middle curve with one electrode above, and one below; right curve with both electrodes below the nervous equator.

Fig. 5 represents the electromyograms obtained from needle electrodes 8 cm. apart in response to a single stimulus (induction shock, administered at the brim of the pelvis). Again, the impulse can be shown to travel at the rate of 29 m. per second.

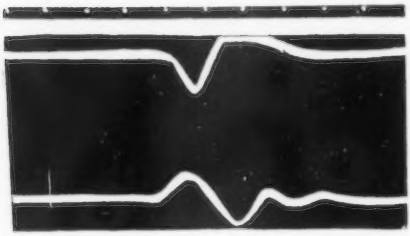

FIG. 4.

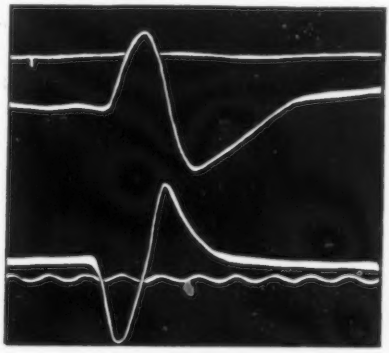

FIG. 5.

. —Electromyogram of knee-jerk led off from two points on the muscle 12 cm. apart. Top line: Time = ·01 sec. Lower record represents response from proximal point.

FIG. 5.—Electromyogram of rectus femoris, in response to break induction shock, recorded by two strings. Lower record represents the response at a point 8 cm. above that recorded by the upper curve. Time = ·01 sec. Uppermost line = stimulus.

The time interval between the responses to stimuli administered at two distant points on a nerve is an expression of the velocity of the

nerve impulse, no other factor being involved; the interval between the action currents led off from two points of a muscle in response to a single stimulus does not only depend on the velocity of conduction of the impulse in the motor nerve, but also on a delay referable to the motor nerve ending. This terminal delay, which has been observed by Fulton, Fuji, Forbes, Ray and Griffith, was attributed by Fulton not to the end-plate, but to diminished conductivity in the finer intramuscular nerve filaments. There is no experimental evidence of such diminished conductivity. Samojloff's assumption of a higher temperature coefficient for the conductivity of the nerve-plate, as against that of the nerve-fibre, would appear to provide an argument against Fulton's view. The so-called end-plate delay is of the order of about one sigma in the mammalian muscle. This factor being now taken into consideration, the discrepancy between the results obtained by the two methods of approach is explained. Turning back to the ulnar nerve experiments, the velocity of conduction was found to be 39 m. per second, or 3·9 sigma elapsed between the muscle contraction in response to the proximal and the distal stimuli. In the quadriceps experiments, the nerve impulse in travelling from one point of the muscle to the other must traverse the motor end-plate. Assuming the end-plate delay to be about one sigma, correction for this brings the apparent velocity of 29 m. to an actual velocity of 39 m. This result shows, incidentally, that there is no grouping of the reflex motor discharges at the proximal and distal points of the muscle. The muscle then does not contract as a whole in the reflex response, although we have reason to believe from the work of Isayama and Fulton that the response is compounded of successive volleys.

The Velocity of Conduction of Afferent Impulses.

A number of experiments were designed and carried out with a view to ascertaining the velocity of conduction on the afferent side. The observation of Hoffmann's, that a single induction shock applied to a motor nerve produces—in the intact human being—a secondary reflex electrical response following on the original direct response, had already led Schäffer to attempt an estimation of the velocity of sensory conduction by stimulating a motor nerve at two points as distant as possible, and noting the time relationship of the reflex responses. The method would appear to be a valid one, since Schäffer clearly showed that the reflex response was not due to a proprioceptive stimulus resulting from the primary contraction, but to actual stimulation of

afferent fibres in the motor nerve itself. The results of Schäffer show, however, such wide variations, that they are valueless. This is to be attributed, *inter alia*, to the impossibility of determining the exact point of stimulation of a deep-seated nerve, such as the sciatic. It seemed possible that stimulation of the ulnar nerve at its two superficial points, and searching for the reflex contraction in each case with the aid of the spring contact breaker, might offer a means of arriving at the velocity in sensory nerve conduction. Numerous experiments, however, failed to detect a secondary reflex response from the abductor minimi digiti muscle, whether the stimulus were a condenser discharge or a break induction shock. One can only conclude that the Hoffmann reflex does not occur in this muscle, but is possibly confined to muscles which are more closely associated with postural function than the small muscles of the hand. The method would appear to be inapplicable in the intact human being, since, unfortunately, nerves supplying postural muscles are mostly deeply seated, and offer at most a single point of access where localized stimulation is possible.

Rate of Conduction and Reflex Times.

The accurate determination of the rate of conduction of motor impulses is only one step in the analysis of the time relations which figure in a reflex response. Velocity of conduction on the afferent side is the second step. There is no warrant for the assumption that afferent conduction takes place at the same rate as efferent. What little is known about the rates of certain types of afferent impulses makes this assumption exceedingly unlikely. Erlanger and Gasser have shown that in the mammal sensory fibres can be divided into two groups: one with a velocity of conduction varying between 30 and 80 m. per second, and one with a velocity of 0·7 to 1·3 per second. Adrian observed that a light touch on the ulnar side of a cat's paw gave rise to impulses of high action potential, probably conducted at a rate of 50 m. per second, or more, and others of less potential, the records of which suggest that they may travel as slowly as 15 to 20 m. per second.

There is some reason for associating fibres conducting impulses of high potential with sensibility to light touch, and those of lower potential with a class of receptor that would give rise to pain on intense stimulation. In the cat, Dennig found a rate of 40 m. for the sensory fibres in the splanchnic, and Eccles and Sherrington a rate of 30 m. for the afferent impulses concerned in the flexor reflex of the leg. Discarding the results of Schäffer, which one is inclined to do on

account of their inconsistencies, no information remains as to the rate of conduction of proprioceptive impulses from tendon joints and muscles. It is certain that until values for afferent conduction are available, comparable in accuracy with at least the present series of motor values, no attempt can be made to calculate the central delay in reflex action. Even when the requisite values for velocity are at hand, a further factor remains for which allowance will have to be made, namely, the continued discharge of a receptor in response to however brief a stimulus. It can only be predicted that, if our values for the rate of motor conduction be accepted, a very much higher rate will have to be assigned to proprioceptive afferent impulses in order to account for the commonly observed values of the latent period of tendon reflexes. Hoffmann, adopting Münnich's figure of 66 m. per second for both afferent and motor conduction, calculated the central delay for the deep reflexes in man, and occasionally obtained negative values. This obvious impossibility would have obtained still more frequently had he made due allowance for the time lost at the receptor organs.

Summary.

A new method is described for the estimation of the velocity of motor nerve impulses in the human subject.

The conduction rate of the ulnar nerve is found to be 38·7 m. per second with a possible error of not more than 5 per cent. The relation of these results to previous estimates and their bearing on the time values of the deep reflexes is discussed.

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NOTE ON THE ACTION OF CURARE IN TETANY.

BY H. HARTRIDGE AND RANYARD WEST.

(From the Physiological Laboratory, St. Bartholomew's Hospital.)

In a recent contribution to this journal [1], the selective removal of the tonic, clonic and fibrillary muscular contractions of parathyroid tetany in the dog was recorded. This was effected by a fresh watery extract of a curare supplied by Messrs. Burroughs Wellcome and Co., who obtained it from an unknown source.

Repetition of this work, with new samples of curare, yielded the following results. Of seven samples tested, two only show the selective action under consideration. In the active samples the selective agent stood boiling and autoclaving, at least in some degree. A watery extract deteriorated, so that the selective action vanished in a few months, leaving the paralytic action, which was, however, somewhat impaired.

It has not been possible to relate the variation in this property of the various curares to their sources in every case, but "Calabash" and "Pot" curares occurred in both groups.

A paper is in course of preparation by one of us [2] showing a similar and parallel variation in the action of curare upon certain rigid conditions in man.

It is not the purpose of this note to consider the theoretical implications of these findings. Bremer, as a result of a very full study [3], [4], [5], [6], [7], of the selective action of curare in decerebrate rigidity and local tetanus, concludes that these are manifestations of Wedenski inhibition, so that "the tonic impulses continuously arriving at the neuromuscular junction of the fibres engaged in postural tone are blocked" at a time when "the junctions of the resting, unfatigued fibres are able to transmit single motor volleys or brief tetanic reflex discharges."

Other theoretical possibilities are dealt with in our previous paper. But at this stage we think it should be suggested that a second active principle may be present either in the principal plant ingredient (usually *Strychnos toxifera*) or in some of the various other ingredients

which contribute to the "curare" which reaches the market. We feel that the time is ripe for a full chemical assay of curare, and this is being undertaken.

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[4] *Idem. Ibid.*, 1927, **97**, 895.
[5] Bremer and Titeca. *Ibid.*, 1928, **99**, 624.
[6] *Idem. Ibid.*, 1931, **107**, 253.
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Notices of Recent Publications.

Les Tumeurs des Centres nerveux et des Nerfs périphériques. (Atlas du Cancer, 9 and 10 fasc.) Par G. Roussy et Ch. Oberling. 12 plates with descriptions. Paris: Félix Alcan. 1931. Price 80 francs.

Under the ægis of the French Association for the Study of Cancer, the authors have given us a monograph on the pathology of the gliomas and neurofibromas richly illustrated with drawings. Although the arrangement is that of an atlas, the twelve large and closely-printed pages of text contain a more detailed histological description of the various types of glioma than is to be found in any textbook. As those who know their work would expect, the authors form their own classification, which differs from that of Bailey and Cushing in several ways. And while certain of the names chosen by these authors, such as "ependymoblastoma" and "glioblastoma" are used, others such as "astroblastoma," "spongioblastoma" "medulloblastoma" and "medullo-epithelioma" are discarded. The authors do not recognize the distinction of the first of these forms from the astrocytomas, considering that the cells which resemble astroblasts are the result rather of the de-differentiation of adult astrocytes than of the perpetuation of the astroblast stage. For this opinion there is considerable justification. But the reason given for classing polar spongioblastomas with the oligodendrogliomas is less clear. As is well known, polar spongioblastomas have been called by Josephy "neurinomes centrales," owing to their resemblance to neurofibromas, and the analogy of the functional resemblance of the sheath of Schwann cells to the oligodendroglia suggests to the authors that central neurinomas might be called "oligodendrocytomes fasciculés." The type of tumour for which the name medulloblastoma is now in general use they call "neurospongioma." There is good reason given for this change in the criticism that the term "medulloblast" is rather a theoretical conception than a recognized cell of the developing neural tube. In any case "medulloblasts" are supposed to appear at a later stage of development than spongioblasts. According to the assumption of Bailey and Cushing, that tumours vary in malignancy according to the stage of development represented by their type cell, medulloblastomas should be less malignant than polar spongioblastomas. But the former are the most malignant and the latter among the least malignant of cerebral tumours. The name "neurospongioma" which the present authors have adopted is less controversial, as it relates to a very early stage of development in which neuroblasts and spongioblasts are not yet fully differentiated. In some

tumours of this type which they have examined the authors have found that the matrix is composed of neurofibrils, and they consider tumours of this type to be related to neuroblastomas rather than to tumours of the neuroglia. Thus included in this alteration of nomenclature there is an altered conception of the nature of the cells forming the tumours. Under the term "neuro-epithelioma" the authors include the primitive medullo-epitheliomas and the rather more differentiated neuro-epitheliomas of the retina. This seems to be an improvement, as all such tumours are rare and gradations between the more primitive and the more differentiated are not uncommon.

Ependymal tumours are classed in three groups, ependymocytomas, ependymoblastomas and ependymogliomas. A clear description is given of these tumours and the various types are well illustrated by the plates.

Perhaps more important than this re-classification is the conception that gliomas do not necessarily grow from cell rests, but may equally well arise as the result of de-differentiation of adult cells. For certain forms, such as the neurospongiomas and neuro-epitheliomas, the authors accept an embryonic origin, but for the others they incline towards the widely accepted view of anaplasia.

In their short chapter on neurofibromas the authors keep to the traditional view of the French school that neurofibromas arise from the sheath of Schwann. They distinguish these growths from plexiform or "true" neuromas, although they accept a similar origin for the latter.

The coloured plates are excellently drawn from sections stained by hæmatoxylin and anilin dyes. The appearances obtained by metallic impregnations are also given in a few line drawings of individual cells. As the authors claim in their preface, it is valuable to be able to say that a microscopic section corresponds to an illustration, whatever may be the name or theory of origin given to the tumour at a later date. It is therefore a little disappointing that many well-known types of tumour, especially of the neuroglial and ependymal groups, are not illustrated. Rather more space is perhaps devoted to the neurospongiomas than is warranted by their variations. There is, however, no limit to the number of possible illustrations in an atlas of the gliomas, and we are very grateful to the authors for succeeding so well in the difficult task to which they set their hands.

Ueber Apraxie: Eine klinische Studie. Von Otto Sittig. Berlin: S. Karger. S. 248. Price 24 M.

For the last thirty years Liepmann's definition and description of apraxia have been generally accepted, though considerable modifications have been suggested in his interpretation of its nature. Some authors have emphasized, even more than Liepmann did, the importance of psychological factors in its pathology; others, as the author of this interesting monograph, have insisted that it should be treated only as a physiological problem and studied by clinical methods rather than by the aid of psychological hypotheses. Sittig calls his volume a "clinical study."

It is a valuable contribution to a subject that needs re-investigation from this point of view. His own observations are recorded in detail, but so clearly and logically that even the long case histories are never tiresome. His arguments are direct and his assumptions rarely go further than his premises warrant. The literature is reviewed critically and used liberally in support of his own observations, in fact the extensive bibliography and the free quotations from other authors will make the book extremely useful to everyone interested in the subject.

Sittig, who has translated some of his papers into German, is familiar with Hughlings Jackson's methods and views and has followed him closely in his treatment of the problems presented by a study of apraxia. He regards apraxia as a disturbance of the more automatic activities, and believes that the lesions to which it is related involve the motor system at a higher functional level than those which produce hemiplegia, etc. In his most interesting case there was a severe apraxia of the trunk, while in others different portions of the body were affected; from these and other observations he concludes that apraxia follows Jackson's law that the most highly organized and complicated activities are first and most severely affected by disease.

Methoden zur Erforschung der Funktionen des Kleinhirns. Von J. TEN CATE. S. 96. Berlin: Urban und Schwarzenberg. 1931. Price 5.50 M.

This monograph forms a part of the volume on "Funktionen des Nervensystems" of Abderhalden's "Handbuch der biologischen Arbeitsmethoden," which is in course of publication. It describes in careful detail the methods of experimentation on the cerebellum which have been, or may be, usefully employed in laboratory animals, and deals more shortly with the observation of the disturbances of function and other phenomena which result from ablation, or mechanical, chemical, and electrical stimulation of the cerebellum. A short description of the mammalian cerebellum and of its chief morphological features in reptiles, birds, and fishes forms a useful introduction to the sections concerned with experimental methods.

Spezielle Chirurgie der Gehirnkrankheiten. Bd. I., Die epileptischen Erkrankungen. Heft 1. Von F. KRAUSE und H. SCHUM. Stuttgart: Ferdinand Enke. 1931. S. 520. Price Rm. 78.

The present is the first of two volumes dealing with its subject from the point of view of the surgeon. It contains a comprehensive, but non-critical, statement of modern knowledge of the incidence, ætiology, symptomatology, physiology and pathology of epileptiform convulsions and of epilepsy proper. A second volume, yet in the press, will deal with diagnosis, medical and surgical treatment and with the social aspects of epilepsy. An extensive and predominantly German bibliography is found at the end of each section.

As a work of reference this volume should prove of value to students of neurology.

Encephalitis Lethargica: its Sequelæ and Treatment. By Constantin von Economo. Translated and adapted by K. O. Newman. Oxford University Press (Humphrey Milford). 1931. Pp. 200, with 21 illustrations. Price 18s.

The German edition of this book was published in 1929 and has been reviewed in these pages. The author has added to this English edition a short section on "Conditions of the Nature of Psychoses"; otherwise the original text is unaltered. The translator has been successful in his difficult task of sailing "between the Scylla of literal translation and the Charybdis of free translation," and the result is both intelligible and readable.

It is evidence of the acuteness of the late Professor von Economo's intellect that so little has had to be changed in our conception of encephalitis lethargica since the publication of his first monograph on the disease in 1918. The descriptton of the sequelæ and of their morbid anatomy had of course to be added, but we know little more either about the ætiology or the morbid anatomy than he told us then. In particular, his conception of the disease as one in which the nerve cells were primarily affected and the inflammatory reactions by the blood-cells were merely secondary concomitants, agrees with the more modern views of virus diseases of the central nervous system. The description of the morbid anatomy in the present volume is indeed by far the most accurate and complete that has appeared in the English tongue. In this section, too, the translator's knowledge of neuropathology has been valuable, as without such knowledge translations of technicalities are apt to be incomprehensible, an error which was not altogether avoided in the English translation of the same author's book on the cerebral cortex.

Die Schädigungen des Nervensystems durch technische Elektrizität. Von F. Panse. S. 155. Berlin: S. Karger. 1930.

Electrical accidents involving the nervous system are now sufficiently common to justify the appearance of this monograph. The author has collected and analysed critically most of the information on the subject available in medical literature, and has added interesting observations of his own.

Symptoms referable to disease of the spinal cord are the most common and interesting, especially the muscular atrophies in regions corresponding to the spinal segments through which the current passed. These are attributed to vasomotor disturbances in the grey matter of the cord due directly to the current, though the fact that weeks or months may intervene between the accident and the onset of the atrophy and palsy often makes this hypothesis difficult to maintain without the assumption of secondary glial changes. Unlike amyotrophic lateral sclerosis, which some of these cases resemble, none progress to a fatal termination. In other cases the spinal symptoms are those of a spastic paresis or of a spastic ataxia, resembling the clinical picture of disseminated sclerosis. Lesions of the peripheral nerves are not

common, though often assumed to be the cause of local palsies and muscular atrophy.

The remarkable resistance of a skull to the passage of a current is probably the explanation of the rarity of cerebral lesions, even when the current has passed through the head: abscesses under a necrosing area of skull are the most common complication, but occasionally signs of local or general cerebral injury are seen. The manner and the immediate cause of death after exposure to electrical currents is also discussed. In view of our uncertainty of the action of electrical currents on the nervous system, this volume is of considerable clinical and pathological interest, and the comprehensive survey of the literature that it contains makes it valuable for reference.

Manuale di Antropologia e Psicologia criminale. Applicata alla Pedagogia emendativa, alla Polizia ed al Diritto penale e penitenziario. Di B. DI TULLIO. Roma: Anonima Romana Editoriale. 1931. Pp. 367. Price L. 35.

The criminal is still the subject of active psychological and anthropological study in the country of Lombroso, and the present work gives a clear account of the conclusions reached there and the general lines of investigation. Dr. di Tullio, who is a lecturer on Criminal Anthropology in the University of Rome, won the Lombroso prize in 1929 with his work "The Delinquent Constitution," of which this is an amplified version. Following a prefatory note by Professor Ottolenghi, the author discusses the place of criminal anthropology in science and social life, its development and present status. The ætiology of crime, the physical and mental characteristics of the criminal from various points of view, biological aspects of crime, classification, prophylaxis and treatment are dealt with enthusiastically and rather discursively, but with a just recognition of the incompleteness of the work so far accomplished. The discussion of the methods of preventing crime, and the author's proposals for limiting it, are of particular interest. There is an alphabetical index of authors quoted, but not of subjects.

Zentralistiche Organisation und Seelenleben. Von JOSEF SCHEIN. München: Ernst Reinhardt. 1931. 2 Bände. S. 448 + 640. Price: Bd. 1, M. 12; Bd. 2, M. 16.

This is an essay in philosophical psychology. The first volume, on postulates, insists on the centralization or unification of psychic life. Among the general problems of habituation and subject-development, impulsive and volitional activity are contrasted, and the importance in mental development of a dominant central organ is emphasized. The second volume deals with the relation of these postulates to psychic processes and consciousness: the problem of perception is studied comprehensively. The book is one for the specialist interested in fundamentals; the author's purpose is to furnish a basis on which psychic happenings, regarded as vital processes and products of development, can be made accessible to objective investigation.

Phantastica. Narcotic and Stimulating Drugs. By LOUIS LEWIN. Translated from the Second German Edition by P. H. A. WIRTH. London: Kegan Paul, Trench, Trübner and Co., Ltd. 1931. Pp. 335. Price 15s.

Lewin's pharmacological investigations have provided the incentive for much important research in psychopathology, and an English translation of his best known book is to be welcomed. Most readers will turn at once to the chapter on Anhalonium Lewinii, where the history, uses and properties of the drug mescalin are set forth; there is interest of a similar kind in the section on Banisteria Caapi and other solanaceæ. The book offers constant evidence of Lewin's wide learning, as well as of his historical and literary interests; it is very readable.

Handbuch der Geisteskrankheiten. Herausgegeben von OSWALD BUMKE. Allg. Teil. 4ter Teil. Berlin: Julius Springer. 1929. S. 421. Price Rm. 44.

This volume concludes the general part of Bumke's system of psychiatry; it deals with therapeutics and jurisprudence.

Professor Vorkastner has written a detailed and well-arranged exposition on forensic psychiatry, which is however concerned only with German, Austrian and Swiss law. It is therefore of little practical use for English readers, but furnishes material for exact comparison with our own legal system in this connection, and is illuminating where it deals with the general problems that occur commonly in occidental countries whenever the psychiatrist is called on for expert testimony.

Dr. Nitsche's section on General Therapy and Prophylaxis is mainly devoted to definite psychotic states, the treatment of the minor forms being taken up by J. H. Schultze in another volume. Dr. Nitsche considers first psychic treatment in the wide sense, and lends little support to those who would restrict the name of psychotherapy to some special procedures of limited application. He discusses occupational therapy, medicinal and dietetic measures, hydrotherapy, seclusion, bed treatment and other problems of institutional care; the medical indications for inducing abortion and for sterilization are examined temperately, as is also the question of the propriety in individual cases of home, rather than institutional, care, with social safeguards and guidance. In a lengthy final chapter prophylaxis is considered. The whole section shows a humane and informed attitude towards matters too often clouded over by prejudice or lukewarmness. The practical details given are precise and helpful.

Professor Birnbaum has written a reflective essay on the branches of knowledge that trench upon psychiatry—cultural and social sciences of various kinds, to which psychopathology is ancillary or receptive. It is a pendant to his systematic study of the historical developments of psychiatry, in volume I

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TO

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